Stereochemistry of the Methoxyphthioceranes

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The phthiocerols, RCH(OMe)·CHMe·$[CH_2]_4$·CH(OH)·CH_2·CH(OH)·$[CH_2]_n$Me (R = Et or Me, n = 20 and 22), constituents of tuberculolipids, have been converted, by substituting H for each OH, into the corresponding methoxyphthioceranes A and B (R = Et or Me, respectively). An optically active diastereoisomer of the latter and structurally related model compounds have been synthesized. By comparison of the methoxyphthioceranes with the synthetic products the asymmetric centres bearing the methoxy-group and the methyl branch are assigned the *threo*-configuration, *threo* being used in the sense defined in *J.C.S. Perkin I*, 1973, 109.

The phthiocerols have been shown [1] to consist of phthiocerol A (I; R = Et) and phthiocerol B (I; R = Me), both being mixtures of homologues with n = 20 and 22. The stereochemistry of the asymmetric centres bearing the hydroxy-groups has been studied earlier.[2] The present paper is concerned with the stereochemistry of the ·CH(OMe)·CHMe· system.

As already briefly reported,[3] the phthiocerols were converted, by reduction of their bistoluene-*p*-sulphonates, into the corresponding mixture of methoxyalkanes, designated methoxyphthioceranes. Separation by preparative t.l.c. gave methoxyphthioceranes A (II;

$$RCH(OMe)\cdot CHMe\cdot [CH_2]_4\cdot CH(OH)\cdot CH_2\cdot CH(OH)\cdot [CH_2]_nMe$$

(I)

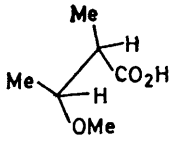
$$RCH(OMe)\cdot CHMe\cdot [CH_2]_{n+7}Me$$

(II)

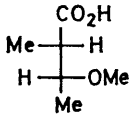
R = Et) and methoxyphthioceranes B (II; R = Me), showing $[\alpha]_D$ −0·5 and −4·1°, respectively.

[1] D. E. Minnikin and N. Polgar, *J. Chem. Soc.* (*C*), 1966, 2107.
[2] K. Maskens, D. E. Minnikin, and N. Polgar, *J. Chem. Soc.* (*C*), 1966, 2113.
[3] K. Maskens and N. Polgar, *Chem. Comm.*, 1970, 673.

The synthesis of one of the stereoisomers of methoxyphthiocerane B (II; R = Me) with $n = 20$ was then undertaken *via* *erythro*-3-methoxy-2-methylbutyric acid (III) [4] as the key intermediate. The terms *erythro* and *threo* are used here in the sense defined in our previous [4] communication. In a Fischer projection the acid (III) would have the formula (IV), and, thus, by the Fischer convention (used in the preliminary note [3]) would be named the *threo*-form.

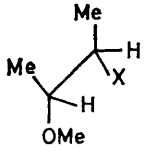


(III)



(IV)

The resolution of the acid (III) has already been described; [4] the partially resolved (—)-acid of about 45% optical purity was employed for the synthesis now described. The methyl ester of this acid was reduced with lithium aluminium hydride, and the resulting alcohol converted into the toluene-*p*-sulphonate. Chain-extension by the malonic ester method gave the (—)-form of the acid (V). The requisite further chain extension was carried out by anodic synthesis. Owing to the very sparing solubility of the sodium salts derived from higher fatty acids two stages were employed. First, anodic coupling of the acid (V) with methyl hydrogen sebacate gave the corresponding stereoisomer of the methoxy-acid (VI) which, on further coupling with nonadecanoic acid was converted into the 2-methoxy-3-methylhentriacontane (VII), showing (45% optical purity) $[\alpha]_D$ —3·0°.



(V) X = $[CH_2]_2 \cdot CO_2H$

(VI) X = $[CH_2]_{10} \cdot CO_2H$

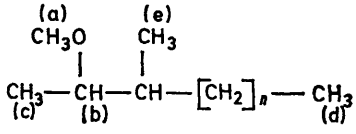
(VII) X = $[CH_2]_{27}Me$

The specific rotation of the synthetic product (VII) (calculated for the optically pure compound: $[\alpha]_D$ —6·7°) was higher than that of methoxyphthiocerane B (—4·1°). Moreover, the n.m.r. spectra showed certain differences (see Table 1). Differences in chemical shift of the protons of the methyl branch and of the terminal methyl group attached to C-2 are of particular relevance; the signals for both groups appear at lower field in the synthetic *erythro*-compound (VII), thus indicating the *threo*-configuration for methoxyphthiocerane B, and hence for the positions 2 and 3 of phthiocerol B.

[4] K. Maskens and N. Polgar, *J.C.S. Perkin I*, 1973, 109.
[5] D. J. Cram and F. A. A. Elhafez, *J. Amer. Chem. Soc.*, 1952, **74**, 5828.

Confirmation of this assignment is provided by the n.m.r. spectrum (Table 2) of a mixture of *threo*- and *erythro*-2-methoxy-3-methyldodecanes (VIII), prepared by methylation of the mixture of alcohols resulting from

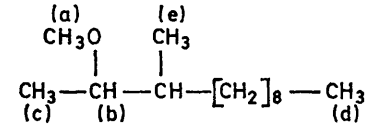
TABLE 1



	Compound (VII) (n = 27)		Methoxyphthiocerane B (n = 27 and 29)	
H	τ	J/Hz	τ	J/Hz
(a)	6·67 (s)		6·67 (s)	
(b)	6·84 (dq)	4·2, 6·2	6·83 (dq)	5·1, 6·3
(c)	8·93 (d)	6·2	8·97 (d)	6·5
(d)	9·12 (t)		9·12 (t)	
(e)	9·13 (d)	6·8	9·17 (d)	6·7

a Grignard reaction between methylmagnesium iodide and 2-methylundecanal. Signals for the protons of the methyl branch and of the terminal methyl group attached to C-2, corresponding to those of both compound (VII) and methoxyphthiocerane B, were clearly distinguished, and for each group of signals the doublet at lower field was clearly more intense. It was expected that the product from the Grignard reaction would contain a preponderance of the *erythro*-secondary alcohol (*cf.* ref. 5), and so the doublet at lower field in each pair of doublets was assigned to the *erythro*-2-methoxy-compound.

TABLE 2



(VIII)

H	τ	J/Hz
(a)	6·68 (s)	
(b)	6·84 (m)	
(c)	8·94 (d)	6·2
	8·97 (d)	6·2
(d)	9·12	
(e)	9·14 (d)	
	9·17 (d)	6·8

It was of interest to attempt the assignment of relative stereochemistry at C-3 and C-4 of phthiocerol A in a similar manner, and the n.m.r. spectrum of methoxyphthiocerane A was compared with that of a model mixture of *threo*- and *erythro*-3-methoxy-4-methyltridecane (IX). The differences in the spectra are less marked than those found for the 2-methoxy-compounds. The methyl branch signal occurs in the synthetic mixture spectrum as a pair of doublets, τ 9·14 and 9·16, the less intense doublet at higher field corresponding with the doublet in the spectrum of methoxyphthiocerane A, and the signal for the protons of the methoxy-group appears in the mixture spectrum as a pair of singlets with a very small separation (0·01 p.p.m.) and the more intense signal at lower field. By detailed comparison of the spectra it

was possible to distinguish in the synthetic mixture spectrum the signals corresponding to methoxyphthiocerane A in the methyl region, and at τ 7·2 for the proton at C-3. Further comparison with the spectrum of a solution containing the synthetic compounds and methoxyphthiocerane A confirmed the spectroscopic assignments, and showed that the latter corresponded with the minor component of the synthetic mixture of *threo*- and *erythro*-isomers. Thus methoxyphthiocerane A, and hence phthiocerol A, possess the *threo*-configuration with respect to C-3 and C-4.

$$MeCH_2 \cdot CH(OMe) \cdot CHMe \cdot [CH_2]_8Me$$

(IX)

Previously it has been suggested [6] that these asymmetric centres have the *erythro*-configuration (*threo*-configuration according to the Fischer convention). This suggestion was based upon the results of demethylation [7] of the phthiocerols with acetic anhydride–toluene-*p*-sulphonic acid, followed by hydrolysis of the product. A triol thus obtained was believed to be identical with a triol resulting on reduction of phthiodiolone (a ketone differing from the phthiocerols in containing a keto-group in place of the methoxy) with sodium borohydride or lithium aluminium hydride. The nature of reactions employed suggests that the products compared were probably mixtures of stereoisomers.

EXPERIMENTAL

Solutions in organic solvents were dried over magnesium sulphate.

Optical rotations were measured with a Perkin-Elmer 141 polarimeter for solutions in chloroform (1% unless otherwise stated). G.l.c. was carried out with a Perkin-Elmer F11 gas chromatograph incorporating a flame ionisation detector (1 m × ⅛ in o.d. steel column packed with 1·5% OV1 at 240°; argon carrier gas at 30 lb in^{-2}). Preparative layer chromatography (p.l.c.) was carried out on 1 m plates (except where otherwise stated) coated with Kieselgel $PF_{254+366}$ 1 mm thick and examined under u.v. light at 366 nm. T.l.c. and unidimensional multiple chromatography (u.m.c.) were carried out on layers of Kieselgel G 0·3 mm thick. Compounds were detected by spraying with sodium dichromate in concentrated sulphuric acid followed by heating at 120°. Silica gel (Whatman Chromedia S.G.31) for column chromatography was activated by heating overnight at 120°.

Petroleum of b.p. 40—60° was used for column chromatography, and petroleum of b.p. 60—80° for t.l.c. and p.l.c.

N.m.r. spectra were determined for solutions in deuteriochloroform with a Perkin-Elmer R14 spectrometer at 100 MHz. Mass spectra were recorded with an A.E.I. MS9 spectrometer.

Methoxyphthioceranes.—Toluene-*p*-sulphonyl chloride (3·5 g, 0·0185 mol) was added in several portions to a stirred, cooled solution of the phthiocerols (3·0 g, *ca.* 0·0056 mol) in pyridine (50 cm^3). Stirring was continued at room temperature for 1 day (whereupon t.l.c. showed the absence of phthiocerols) and water (0·5 cm) was added to hydrolyse unchanged toluene-*p*-sulphonyl chloride. The solution was poured on a mixture of ice (150 g) and concentrated hydrochloric acid (70 cm^3), and extracted with ether. The ethereal solution was washed successively with 2M-hydrochloric acid, water, and saturated sodium chloride solution, dried, and evaporated to give a mixture. A solution of the products (4·3 g) in ether (30 cm^3) was added to a stirred solution of lithium aluminium hydride (1·0 g) in ether (100 cm^3) and the mixture was boiled for 5 h. Unchanged lithium aluminium hydride was destroyed with ethyl acetate (2 cm^3), 2M-hydrochloric acid was added, and the ethereal solution was separated, washed successively with 5% sodium carbonate solution, water, saturated sodium chloride solution, dried, and evaporated. *p*-Tolylsulphonylation and reduction was repeated to give a mixture (2·56 g) containing methoxyphthioceranes A and B with a trace of a polar contaminant [u.m.c., petroleum–ether (98 : 2); 3 passes, R_F 0·72, 0·64, 0·03].

The mixture was chromatographed on silica gel (70 g). After development with petroleum (500 cm^3) and petroleum–ether (199 : 1; 400 cm^3), elution with petroleum–ether (99 : 1; 1200 cm^3) gave materials collected in six fractions. The first two fractions contained methoxyphthiocerane A (0·571 g) and the remaining fractions contained a mixture of methoxyphthioceranes A and B (1·63 g). Some of this mixture (0·968 g) was subjected to p.l.c. [5 plates, petroleum–ether (99 : 1); 6 passes]; two bands were removed from the plates and extracted with ether. The first band gave (−)-methoxyphthiocerane A (0·915 g), m.p. 57°, $[\alpha]_D^{20}$ −0·5° (*c* 13·8) [u.m.c., petroleum–ether (98 : 2); 3 passes, R_F 0·72. homogeneous], τ 6·65 (3H, s, OMe), 7·12 (1H, m, EtC*H*OMe·CHMe·), and 9·0—9·2 (9H, methyls), *m/e* 521 (*M* − 1, 0·2%), 507 (*M* − Me, 0·2%), 493 (*M′* − 1 and *M* − 29, 6%), 479 (*M′* − Me, 1·5%), 465 (*M′* − 29, 17%), and 73 ($EtCHOMe^+$, 100%). G.l.c. showed two components, t_R 9·3 (42%) and 15·7 min (58%). Combined g.l.c. and mass spectrometry showed, for the two components, highest mass peaks at *m/e* 462 and 490 respectively, corresponding to homologous methoxyphthioceranes A after loss of methanol.

The second band yielded material (0·048 g) which still contained a small amount of methoxyphthiocerane A and was subjected to further p.l.c. [1 plate 20 × 20 cm, petroleum–ether (99 : 1); 3 passes then 98 : 2, 3 passes]. Extraction of the main band gave (−)-methoxyphthiocerane B (0·023 g), m.p. 57·5—58°, $[\alpha]_D^{20}$ −4·1° [u.m.c., petroleum–ether (98 : 2); 3 passes, R_F 0·64, homogeneous], *m/e* 507 (*M* − 1, 0·8%), 493 (*M* − 15, 2%), 479 (*M′* − 1, 5%), 476 (*M* − 32, 8%), 448 (*M′* − 32, 15%), 420 (*M′* − 60, 8%), and 59 ($MeCHOMe^+$, 100%). G.l.c. showed two components, t_R 7·5 (37%) and 12·6 min (63%).

(+)-erythro-3-*Methoxy*-2-*methylbutan*-1-*ol*.— Methyl *erythro*-3-methoxy-2-methylbutyrate [4] (6·42 g, 0·044 mol; $[\alpha]_D^{20}$ −4·0°) in dry ether (15 cm^3) was added during 0·5 h to a stirred, ice-cooled solution of lithium aluminium hydride (1·2 g, 0·032 mol) in dry ether (180 cm^3). The mixture was stirred at room temperature for 1 h then boiled for 15 min. Unchanged lithium aluminium hydride was decomposed and the product was isolated as in the preceding section. Distillation gave (+)-erythro-3-*methoxy*-2-*methylbutan*-1-*ol* (4·82 g, 92%), b.p. 164° at 760 mmHg, n_D^{20} 1·4235, $[\alpha]_D^{20}$ +11·2°, τ 6·33 and 6·49 (2H, dd, *J* 10·5 and 7·0 Hz and dd, *J* 10·5 and 5·5 Hz, ·C*H*$_2$·OH), 6·74 (1H, dq, *J* 6·3 and 3·6 Hz,

[6] J. Asselineau, 'The Bacterial Lipids,' Hermann, Paris, 1966, p. 77.

[7] H. Demarteau-Ginsburg and E. Lederer, *Compt. rend.*, 1955, **240**, 815.

·C*H*·OMe), 6·93 (3H, s, OMe), 7·25br (1H, s, ·CH_2·O*H*), 8·26 (1H, m, ·C*H*Me·CH_2·OH), 9·04 (3H, d, *J* 6·3 Hz, terminal Me), and 9·16 (3H, d, *J* 7·1 Hz, methyl branch), *m/e* 118 (*M*, 0·2%), 117 (*M* − 1, 0·2%), 103 (*M* − 15, 2%), 100 (*M* − 18, 1%), and 59 ($MeCHOMe^+$, 100%).

(+)-erythro-3-*Methoxy*-2-*methylbutyl Toluene*-p-*sulphonate*.—Toluene-*p*-sulphonyl chloride (9·30 g, 0·049 mol) was added in several portions during 0·5 h to an ice-cooled, stirred solution of *erythro*-3-methoxy-2-methylbutan-1-ol (4·80 g, 0·041 mol; $[\alpha]_D^{20}$ +11·2°) in pyridine (40 cm^3). The solution was stirred at room temperature for 2 h, water (0·5 cm^3) was added, and stirring was continued for 10 min. The product was isolated in the usual way to give (+)-erythro-3-*methoxy*-2-*methylbutyl toluene*-p-*sulphonate* (9·80 g, 88%), n_D^{20} 1·5000, $[\alpha]_D^{20}$ +3·3° (Found: C, 57·6; H, 7·2; S, 11·4. $C_{13}H_{20}O_4S$ requires C, 57·4; H, 7·4; S, 11·8%), τ 2·20 (2H, d, *J* 8·5 Hz, aryl H), 2·65 (2H, d, *J* 8·5 Hz, aryl H), 5·94, 6·14 (2H, dd, *J* 9·4 and 6·7 Hz, and dd, *J* 9·4 and 6·4 Hz, ·CH_2·OTs), 6·65 (1H, m, MeC*H*·OMe), 6·80 (3H, s, OMe), 7·55 (3H, s, Ar*Me*), 8·09 (1H, m, ·C*H*Me·CH_2·OTs), 8·95 (3H, d, *J* 6·4 Hz, terminal Me), and 9·12 (3H, d, *J* 7·1 Hz, methyl branch), *m/e* 272 (*M*, 0·1%), 100 (*M* − TsOH, 10%), 59 ($MeCHOMe^+$, 100%). T.l.c. [petroleum–ether (60 : 40)] showed the material to be homogeneous, R_F 0·40.

threo-3-*Methoxy*-2-*methylbutyl Toluene*-p-*sulphonate*.—Similarly, a mixture of approximately equal amounts of *threo*- and *erythro*-3-methoxy-2-methylbutan-1-ols (3·54 g) was converted into the corresponding mixture of toluene-*p*-sulphonates (6·84 g, 84%), shown by t.l.c. to contain two components, R_F 0·40 and 0·37. The mixture was chromatographed on silica gel (150 g). After development with petroleum–ether (9 : 1; 1000 cm^3), elution was continued with petroleum–ether (4 : 1; 400 cm^3 and 3 : 1; 1000 cm^3). Fractions (100 cm^3) were collected and material was isolated from the last 13 fractions. Fractions 1—8 (5·67 g) contained both isomers and fractions 9—13 (0·72 g) contained almost entirely the *threo*-isomer. This material was subjected to p.l.c. [3 plates, petroleum–ether (9 : 1); 6 passes] to give threo-3-*methoxy*-2-*methylbutyl toluene*-p-*sulphonate* (0·62 g), n_D^{20} 1·4987 (Found: C, 57·6; H, 7·6; S, 11·5. $C_{13}H_{20}O_4S$ requires C, 57·4; H, 7·4; S, 11·8%), τ 5·97 (2H, d, *J* 5·5 Hz, CH_2·OTs), 6·92 (quintet, *J* 6·5 Hz, ·C*H*·OMe), and 8·14 [1H, m, ·CH(OMe)·C*H*Me]; other signals were the same as those for the *erythro*-isomer and the mass spectrum was similar to that of the *erythro*-isomer.

(−)-erythro-5-*Methoxy*-4-*methylhexanoic Acid*.—Sodium (1·15 g, 0·05 mol) was dissolved in dry ethanol (50 cm^3). Diethyl malonate (8 g, 0·05 mol) in ethanol (25 cm^3) was added to the warm solution, followed after 15 min by *erythro*-3-methoxy-2-methylbutyl toluene-*p*-sulphonate (13·6 g, 0·05 mol; $[\alpha]_D^{20}$ +3·3°) in ethanol (25 cm^3). Sodium iodide (1·0 g) was added and the mixture was boiled for 20 h. Most of the ethanol was evaporated off; the residue was dissolved in water, acidified, and extracted with ether. The ethereal solution was washed with sodium thiosulphate solution and water, dried, and evaporated. The crude product was hydrolysed with potassium hydroxide (20 g) in water–ethanol (7 : 2; 200 cm^3) by boiling for 4 h. The solution was diluted with water, extracted with ether to remove unhydrolysed material, acidified, and extracted with ether. The ethereal solution of acidic material was washed with water, dried, and evaporated to give the substituted malonic acid (7·7 g). This material was heated at 150° (bath) for 40 min; the products were dissolved in ether and extracted with 2M-sodium hydroxide solution. The separated alkaline solution was acidified and extracted with ether. The ethereal solution was washed with water, dried, and evaporated. Distillation of the residual liquid gave (−)-erythro-5-*methoxy*-4-*methylhexanoic acid* (3·8 g, 48%), b.p. 109° at 0·4 mmHg, n_D^{24} 1·4380, $[\alpha]_D^{20}$ −4·4°, τ 6·69 (3H, s, OMe), 6·80 (1H, dq, *J* 6 and 4 Hz, MeC*H*·OMe), 7·83 (2H, m, CH_2·CO_2H), 8·90 (3H, d, *J* 6·2 Hz, terminal methyl), and 9·10 (3H, d, *J* 6·5 Hz, methyl branch), *m/e* 145 (*M* − 15, 2%) and 59 ($MeCHOMe^+$, 100%).

threo- *and* erythro-5-*Methoxy*-4-*methylhexanoic Acids*.—In a similar manner a mixture of *threo*- and *erythro*-3-methoxy-2-methylbutyl toluene-*p*-sulphonates gave *threo*- and *erythro*-5-methoxy-4-methylhexanoic acids, b.p. 150—151° at 20 mmHg, n_D^{26} 1·4370 (Found: C, 59·7; H, 10·1. Calc. for $C_8H_{16}O_3$: C, 60·0; H, 10·1%). In addition to signals for the *erythro*-isomer the n.m.r. spectrum showed τ 8·92 (d, *J* 6·2 Hz, terminal methyl) and 9·12 (d, *J* 6·5 Hz, methyl branch).

erythro-13-*Methoxy*-12-*methyltetradecanoic Acid*.—Methyl hydrogen decanedioate (2·50 g, 0·0118 mol) and (−)-*erythro*-5-methoxy-4-methylhexanoic acid (1·90 g, 0·0118 mol; $[\alpha]_D^{20}$ −4·4°) were dissolved in a solution of sodium methoxide [from sodium (0·54 g, 0·0236 mol)] in methanol (150 cm^3). The solution was electrolysed in a water-cooled cell with a mercury cathode and a rotating platinum anode of 2·5 cm diam., at *ca.* 1 A. After a few min the current fell to 0·5 A and electrolysis was continued for 1 h. The solution was decanted from the mercury and together with washings was evaporated to remove most of the methanol. The residue was portioned between 2M-sodium hydroxide solution and ether. The ethereal solution was washed with water, dried, and evaporated to give neutral products (1·92 g).

The neutral material was hydrolysed by boiling with potassium hydroxide (2·5 g) in water (25 cm^3) and ethanol (5 cm^3). Unhydrolysed material (0·30 g) was extracted with ether; acidification of the alkaline solution followed by ether extraction gave a mixture of acidic products (1·48 g). This mixture was digested with petroleum and most of the dibasic acid was removed by filtration. Evaporation of the filtrate gave a residue which was combined with material from another electrolysis (total 1·33 g) and subjected to p.l.c. [5 plates, petroleum–ether–acetic acid (60 : 40 : 0·5); 3 passes]. The main band gave essentially *erythro*-13-methoxy-12-methyltetradecanoic acid (0·78 g). Combined g.l.c. and mass spectroscopy of the methyl ester showed *m/e* 271 (*M* − Me, 1%), 255 (*M* − OMe, 1%), 226 (*M* − 60, 1%), 199 (*M* − 87, 1·3%), and 59 ($MeCHOMe^+$, 100%).

(−)-erythro-2-*Methoxy*-3-*methylhentriacontane*.—Nonadecanoic acid (0·90 g, 0·0030 mol) and *erythro*-13-methoxy-12-methyltetradecanoic acid (0·62 g, 0·0023 mol) were added to a solution of sodium methoxide [from sodium (0·122 g, 0·0053 mol)] in methanol (30 cm^3) and petroleum (20 cm^3). Electrolysis was carried out as described previously. The decanted solution was acidified with hydrochloric acid and evaporated, and the residue was partitioned between water and petroleum. The petroleum solution was washed with water, dried, and evaporated to give a residue (1·36 g) shown by t.l.c. [petroleum–ether (9 : 1)] to contain four main components, R_F 0·82, 0·63, 0·40, and 0·05.

The residual mixture was chromatographed on silica gel (70 g). Elution with petroleum gave hexatriacontane (0·327 g), m.p. 77—77·5° (from chloroform); petroleum–

ether (98 : 2) gave material which was mainly the required product (0·272 g, 25%); petroleum–ether (96 : 4) gave mainly the self-coupled ether (0·050 g, 5%); further elution with more polar solvents gave material (0·680 g) containing the starting acids.

The crude cross-coupled product was subjected to p.l.c. [1 plate, petroleum–ether (199 : 1); 2 passes then 99 : 1; 3 passes] to give (—)-erythro-2-*methoxy*-3-*methylhentriacontane* (0·118 g), m.p. 55·5—56°, $[\alpha]_D^{20}$ —3·0, *m/e* 480 (*M*), 479 (*M* — 1), 465 (*M* — 15), 448 (*M* — 32), 420 (*M* — 60), and 59 ($MeCHOMe^+$, 100%). U.m.c. [petroleum–ether (98 : 2); 3 passes] showed the material to be homogeneous. G.l.c. showed one peak, t_R 7·5 min, corresponding to the lower homologue present in methoxyphthiocerane B.

The crude self-coupled product was subjected to p.l.c. [1 plate 20 × 20 cm, petroleum–ether (95 : 5); 3 passes] to give *erythro*-2,25-dimethoxy-3,24-dimethylhexacosane (0·024 g), m.p. 28—29°, τ 6·68 (6H, s, OMe), 6·84 (2H, dq, *J* 6 and 4 Hz, ·C*H*·OMe), 8·93 (6H, d, *J* 6 Hz, terminal methyl), and 9·14 (6H, d, *J* 7 Hz, methyl branch), *m/e* 454 (*M*), 453 (*M* — 1), 439 (*M* — 15), 422 (*M* — 32), 395 (*M* — 59), 330 (*M* — 64), and base peak 59 ($MeCHOMe^+$).

2-*Methoxy*-3-*methyldodecane* (VIII).—A Grignard reaction between 2-methylundecanal and methylmagnesium iodide gave 3-*methyldodecan*-2-*ol*, b.p. 129—130° at 9 mmHg, n_D^{19} 1·4458 (Found: C, 77·5; H, 13·8. $C_{13}H_{28}O$ requires C, 77·9; H, 14·1%), τ 6·28 (1H, m, ·C*H*·OH), 8·50 (1H, s, ·O*H*), 8·85 and 8·88 (two doublets, *J* 6·5 Hz, *Me*CH·OH), 9·12 (t, *Me*CH_2·), and 9·12 and 9·14 (two doublets, *J* 7 Hz, methyl branch), *m/e* 199 (*M* — 1, 0·3%), 185 (*M* — 15, 2%), 182 (*M* — 18, 5%), 154 (*M* — 46, 15%), and 45 ($MeCHOH^+$, 100%). This was methylated by the following procedure.

Sodium hydride dispersion (0·5 g, 0·01 mol) was stirred with dimethyl sulphoxide (6 cm^3) under nitrogen at 65° for 1 h. A solution of 3-methyldodecan-2-ol (2·0 g, 0·01 mol) in dimethyl sulphoxide (2 cm^3) was added to the cooled mixture and stirring was continued at 40° for 1 h. Methyl iodide (1·54 g, 0·01 mol) was added to the cooled mixture and stirring was continued overnight. The mixture was poured into water and extracted with methylene chloride. The extract was washed repeatedly with water, dried, and evaporated. Chromatography of the residual liquid on silica gel gave, on elution with petroleum–ether (95 : 5) 2-*methoxy*-3-*methyldodecane* (1·53 g, 72%), b.p. 119° at 10 mmHg, n_D^{18} 1·4340 (Found: C, 78·4; H, 13·8. $C_{14}H_{30}O$ requires C, 78·4; H, 14·1%), *m/e* 214 (*M*, 0·05%), 213 (*M* — 1, 0·1%), 199 (*M* — 15, 0·4%), 182 (*M* — 32, 0·4%), 154 (*M* — 60, 2%), and 59 ($MeCHOMe^+$, 100%).

3-*Methoxy*-4-*methyltridecane* (IX).—A Grignard reaction between 2-methylundecanal and ethylmagnesium bromide gave 4-*methyltridecan*-3-*ol* (58 g, 90%), b.p. 139° at 8 mmHg, n_D^{19} 1·4482 (Found: C, 78·4; H, 13·9. $C_{14}H_{30}O$ requires C, 78·4; H, 14·1%), *m/e* 213 (*M* — 1, 0·2%), 196 (*M* — 18, 1%), 185 (*M* — 29, 6%), 154 (*M* — 60, 3%), and 59 ($EtCHOH^+$, 100%). Methylation as in the preceding section afforded 3-*methoxy*-4-*methyltridecane* (2·05 g, 90%), b.p. 138° at 12 mmHg, n_D^{21} 1·4330 (Found: C, 78·7; H, 14·0. $C_{15}H_{32}O$ requires C, 78·9; H, 14·1%), *m/e* 228 (*M*, 0·06%), 227 (*M* — 1, 0·15%), 199 (*M* — 29, 7%), and 73 ($EtCHOMe^+$, 100%).

In a preliminary model experiment 3-*methoxy*-4-*methylheptane* was prepared *via* 4-methylheptane-3-ol by methylation as before. It had b.p. 40° at 9 mmHg, n_D^{24} 1·4110 (Found: C, 75·0; H, 13·7. $C_9H_{20}O$ requires C, 74·9; H, 14·0%), τ 6·65 and 6·67 (3H, two singlets, OMe), 7·10 (1H, m, C*H*·OMe), and 9·0—9·2 (9H, methyls), *m/e* 144 (*M*, 0·2%), 115 (*M* — 29, 12%), and 73 ($EtCHOMe^+$, 100%).

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