The Chemistry of Fungi. Part LXXIII.[1] Some Derivatives of 5-Ethyl-2,5-dimethylcyclohexanone

By **Anthony R. Greenaway** and **W. Basil Whalley,*** The School of Pharmacy, The University of London, London WC1N 1AX

Methylation of the pyrrolidine enamine of (±)-3-ethyl-3-methylcyclohexanone yields a mixture of the geometrical isomers, (±)-5-ethyl-*trans*- and (±)-5-ethyl-*cis*-2,5-dimethylcyclohexanone. The earlier suggestion that the second methylation product was (±)-3-ethyl-2,3-dimethylcyclohexanone is incorrect. These *cis*- and *trans*-cyclohexanones have been separated and characterised. The corresponding cyclohexanols have been prepared.

IN connection with our synthesis of 5-ethyl-2,5-dimethyl-cyclohexanone (1), a degradation product of the fungal metabolite rosenonolactone, we have previously reported [2] the methylation of the pyrrolidine enamine of (±)-3-

ethyl-3-methylcyclohexanone (2). In addition to the desired methylation product (1), a second, isomeric substance was obtained and formulated [2] as (±)-3-ethyl-2,3-dimethylcyclohexanone (3). Since the formation of

[1] Part LXXII, J. S. Millership, J. M. Midgley, and W. B. Whalley, preceding paper.

[2] J. N. T. Gilbert, A. J. Hannaford, L. Minami, and W. B. Whalley, *J. Chem. Soc.*, 1966, 627.

(3) was not anticipated on general grounds,[3] we have recently re-examined our earlier conclusion: it is now clear that structure (3) is incorrect and that the two isomeric cyclohexanones are the (±)-*cis*- and (±)-*trans*-isomers (4) and (5), respectively.

Thus the enamine from pyrrolidine and (±)-3-ethyl-3-methylcyclohexanone contained the isomeric derivatives (6) and (7), as indicated by the n.m.r. spectrum (benzene) which had signals at τ 5.70 [1 H, t, in (7)] and 5.93 [1 H, s, in (6)], in the ratio 65 : 35. This ratio changed to 75 : 25 on addition of catalytic amounts of toluene-*p*-sulphonic acid to the mixture of enamines. This result is similar to the 80 : 20 ratio for the corresponding isomeric pyrrolidine enamines from 3,3-dimethylcyclohexanone, as estimated [4] by ozonolysis of the mixture and determination of the relative amounts of the resultant dicarboxylic acids (8) and (9).

The isomers (4) and (5) were separated by preparative g.l.c. (see Experimental section), and obtained as stable, homogeneous liquids. The n.m.r. spectra were particularly informative since the C-6 methylene protons in (4) exhibited a signal at τ 7.85, whereas the corresponding signal for (5) was at τ 7.80 (both broad singlets). These
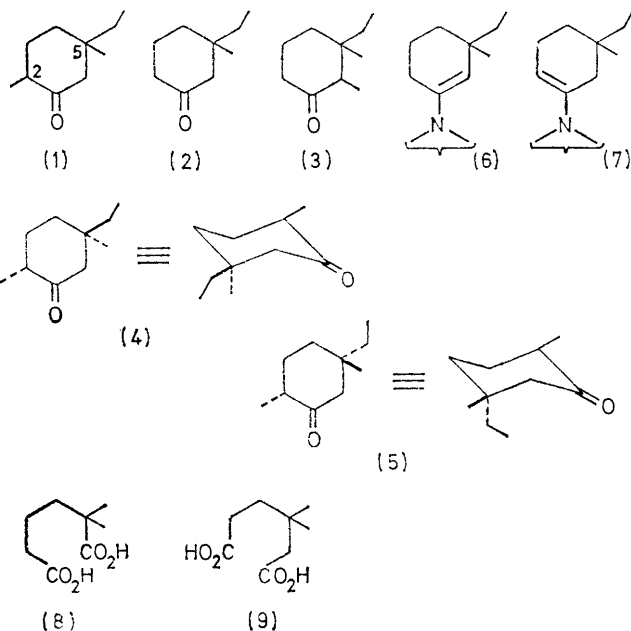
geometrical isomers were unchanged on t.l.c. and g.l.c. but were quickly equilibrated by acid or base to a mixture of (4) and (5) in the ratio 54 : 46. The more stable isomer is thus regarded on general principles as the *cis*-compound (4). This assignment is also compatible with the n.m.r. spectral data: the equatorial C-5 methyl

[3] G. Stork, A. Brizzolara, H. Landesman, J. Szmuskovicz, and R. Terrell, *J. Amer. Chem. Soc.*, 1963, **85**, 207; G. Stork and S. R. Dowd, *ibid.*, p. 2178; J. A. Marshall and N. Cohen, *ibid.*, 1965, **87**, 2773; J. A. Marshall, N. Cohen, and A. R. Hochstetler, *ibid.*, 1966, **88**, 3408.

[4] J. Champagne, H. Favre, D. Vocelle, and I. Zbikowski, *Canad. J. Chem.*, 1964, **42**, 212.

[5] N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden–Day, San Francisco, 1964; R. F. Zurcher, *Helv. Chim. Acta*, 1963, **46**, 2054.

group in (4) exhibits a signal at τ 9.02, downfield from the corresponding signal for the axial C-5 methyl group (τ 9.17) in (5) (*cf.* ref. 5).

Although the more stable *cis*-isomer predominates in the equilibrium mixture of (4) and (5), the product isolated directly from the methylation procedure contains more (55% as determined by g.l.c. and n.m.r.) of the less stable *trans*-isomer. This is in accord with, for example, the production [6] of the less stable *trans*-2,4-dialkylcyclohexanones as the major products from the alkylation of the pyrrolidine enamines of 4-alkylcyclohexanones.

The mass spectra of (4) and (5) are identical and show intense ions at m/e 154 (M^+), 125 ($M - 29$), 110 ($M - 44$, 14%), 97 ($M - 57$), 55, and 41. The peak at m/e 110 provides convincing collateral evidence for the structure of (4) and (5), since the fragmentation pattern for α-methylcyclohexanones devoid of substituents at C-6 is particularly characteristic.[7]

To provide additional evidence for our conclusions two additional routes to the ketones (4) and (5) were used. In the first, (±)-3-ethyl-3-methylcyclohexanone was converted by way of the 6-hydroxymethylene derivative into the 6-butylthiomethylene derivative (10). Reduction of this compound with Raney nickel gave a mixture of (4) and (5) contaminated by the corresponding alcohols. Oxidation of the total product with Jones reagent gave a mixture of (4) and (5) which was separated by g.l.c.; the products were identical (i.r., u.v., n.m.r., and mass spectra, t.l.c., and g.l.c.) with the previously obtained ketones.

In the second process, 3,6-dimethylcyclohex-2-enone was ethylated by conjugate addition of lithium diethylcuprate, to yield products identical with (4) and (5).

Since the separation of (4) and (5) by preparative g.l.c. was tedious and time-consuming, an alternative approach designed to prepare the cyclohexanones in quantity was employed. Thus reduction of the equilibrium mixture of (4) and (5) with lithium aluminium hydride gave the four diastereoisomeric alcohols (11)—(14), in which the axially oriented hydroxy-isomers [8] [complex multiplet in n.m.r. at τ 6.10, CH·OH (equatorial)] predominated over the equatorially oriented hydroxy-isomers [8] [broad multiplet in n.m.r. at τ 6.65, CH·OH (axial)] in the ratio 82 : 18 (by integration). These four isomers were separable by g.l.c. (Experimental section), and were stable to g.l.c. and t.l.c. (confirmed by repeated recycling). Compounds (12) and (11) were further characterised as the distinctive, and different, hydrogen 3-nitrophthalates, in which it would appear likely that conformational inversion to place the ester group in an equatorial conformation has occurred. The stability of these four alcohols in the conformations illustrated as opposed to the alternative 'inverted' conformations, is in accord with general conformational

[6] S. Karady, M. Lenfant, and R. E. Wolff, *Bull. Soc. chim. France*, 1965, 2472.

[7] S. Seibl and T. Gaumann, *Z. analyt. Chem.*, 1963, **197**, 33; *Helv. Chim. Acta*, 1963, **46**, 2857.

[8] J. C. Richer and D. Perelman, *Canad. J. Chem.*, 1966, **44**, 2003.

principles. Oxidation by the Sarrett reagent of the alcohols (11)—(13) regenerated (quantitatively) the corresponding ketones. As a further check on the
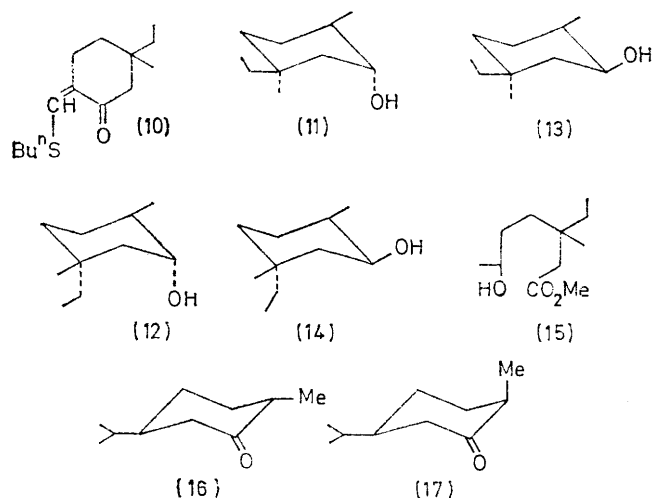
purity of (4) and (5) obtained by this route, and to confirm that no inversion occurred at C-2 during the oxidation, the ketones were reduced by lithium hydrido-trimethoxyaluminate and yielded (quantitatively) the alcohols (11) and (12), respectively: g.l.c. on Apiezon and Diglycerol indicated the absence of other diastereo-isomeric alcohols.

Baeyer–Villiger oxidation of the cyclohexanones (4) and (5) gave (quantitatively) the corresponding, different, *cis*- and *trans*-ε-lactones (i.r., u.v., n.m.r., and mass spectra, t.l.c., and g.l.c.) each of which formed the same methyl 3-ethyl-3-methyl-6-hydroxyheptanoate (15).

All these facts are compatible with the view that compounds (4) and (5) are geometrical isomers and not conformers [*cf.*, for example, the similar situation [9] with carvomenthone (16) and isocarvomenthone (17)].

In accord with our previous report,[2] the mixture of (4) and (5) gives the (±)-oxime and (±)-2,4-dinitro-phenylhydrazone, which (after purification) correspond to the (±)-*cis*-ketone (5); *cf.* the similar behaviour of the naturally derived ketone. This observation is compatible with the *cis*-isomer reacting more readily than the *trans*-isomer, and with the apparent greater solubility of the derivatives of the *trans*-isomer.

EXPERIMENTAL

Unless otherwise stated i.r. spectra were determined for Nujol mulls. U.v. spectra were recorded for solutions in 96% ethanol. N.m.r. spectra were determined for solutions in deuteriochloroform with Me_4Si as internal standard. Silica for chromatography was Hopkin and Williams HFC grade; alumina was Spence type 1. T.l.c. was conducted with Kieselgel GF_{254} in layers of 0.3 mm thickness. G.l.c. was performed with flame ionisation detection, and nitrogen as carrier gas. Details of columns are recorded in the text together with (*a*) column temperature (°C), (*b*) the rate of flow of the mobile phase (in ml min⁻¹), and (*c*) the retention time (t_R/min), corrected for the dead-space volume by injection of air. Accurate mass measurements were carried out at a resolving power of 4 000 (10% valley definition).

(±)-5-*Ethyl*-trans   and   (±)-5-*Ethyl*-cis-2,5-*dimethyl-cyclohexanone.—Method A*. 3-Methylcyclohex-2-enone [2] had b.p. 60° at 3 mmHg (Found: C, 76.0; H, 9.4. Calc. for $C_7H_{10}O$: C, 76.3; H, 9.2%). T.l.c. on silica and alumina, both developed with benzene–ethyl acetate (4 : 1), showed single spots of R_F 0.45 and 0.70, respectively. G.l.c. on Apiezon L (161°; 180 ml min⁻¹ N_2) showed one component. The 2,4-*dinitrophenylhydrazone*, which formed red plates, m.p. 172° (from ethanol) (Found: C, 53.6; H, 5.0; N, 19.1. $C_{13}H_{14}N_4O_4$ requires C, 53.8; H, 4.9; N, 19.3%), was homogeneous on silica, developed with benzene (R_F 0.55).

3-Methylcyclohex-2-enone was converted into 3-ethyl-3-methylcyclohexanone by the following improvement of the reported process.[10] Ethyl bromide (135 ml) dissolved in ether (300 ml) was added with stirring, at −10 °C, to finely divided lithium (2.8 g) (under nitrogen). If necessary, addition of ethyl bromide was interrupted after about 10% had been introduced to allow the initiation of the formation of ethyl-lithium. When formation of ethyl-lithium was complete, the solution was transferred (stirring; nitrogen) to a suspension of copper(I) iodide (130 g) in ether (200 ml) at 0 °C. When formation of the brown solution of lithium diethylcuprate was complete a solution of 3-methylcyclohex-2-enone (40 g) in ether (100 ml) was added. After 1 h (with stirring) the mixture was poured into saturated aqueous ammonium chloride (1 l). The ethereal layer was isolated, washed, dried, and distilled to yield (±)-3-ethyl-3-methyl-cyclohexanone (40 g), b.p. 75° at 7.3 mmHg (lit.,[10] 97—98° at 22 mmHg) (Found: C, 77.4; H, 11.4%; M^+, 140. Calc. for $C_9H_{16}O$: C, 77.1; H, 11.5%; M, 140). G.l.c. on Apiezon L (161°; 180 ml min⁻¹ N_2) showed the presence of one component, t_R 29.4 min. T.l.c. on silica [developed with benzene–ethyl acetate (9 : 1)] showed one spot, R_F 0.55; $\nu_{max.}$ (film) 1 710s cm⁻¹. The semicarbazone formed needles, m.p. 182° (from methanol) (Found: C, 61.0; H, 9.6; N, 21.5. Calc. for $C_{10}H_{19}NO$: C, 60.9; H, 9.7; N, 21.3%) (lit.,[10] m.p. 181—181.5°). The 2,4-*dinitrophenylhydrazone* formed orange plates, m.p. 94—96° (from methanol) (Found: C, 55.7; H, 6.1; N, 16.5. $C_{15}H_{20}N_4O_4$ requires C, 56.2; H, 6.3; N, 17.4%).

A solution of (±)-3-ethyl-3-methylcyclohexanone (25 g) and pyrrolidine (29 g) in benzene (100 ml) was refluxed (with continuous removal of water) until formation of enamines [monitored by disappearance of i.r. band at $\nu_{max.}$ 1 710 cm⁻¹ (carbonyl) and appearance of that at $\nu_{max.}$ 1 643 cm⁻¹ (enamine)] was complete (8 h). Purified by distillation, the product (30 g), b.p. 112° at 4.4 mmHg contained (±)-1-pyrrolidino-5-ethyl-5-methylcyclohexene and (±)-1-pyrroli-dino-3-ethyl-3-methylcyclohexene in the ratio (65 : 35) (see n.m.r. data) (Found: C, 80.8; H, 12.3. Calc. for $C_{13}H_{23}N$: C, 80.8; H, 12.0%), $\lambda_{max.}$ (cyclohexane) 227 nm (log ε 3.84), τ 5.70 (0.65 H) and 5.93 (0.35 H).

A solution of this mixture of enamines (25 g) in benzene (100 ml) containing methyl iodide (25 g) was refluxed for 24 h. Water (40 ml) was added and the mixture was boiled for a further 1 h; the cooled solution was then acidified with an excess of 2N-sulphuric acid. After isolation with ether followed by fractional distillation, the mixture of (±)-*trans*- and (±)-*cis*-5-ethyl-2,5-dimethylcyclohexanones was obtained as an oil (9.1 g), b.p. 82—84° at 9.3 mmHg (Found: C, 77.8; H, 11.7%; M^+, 154. Calc. for $C_{10}H_{18}O$: C, 77.9;

[9] R. G. Johnston and J. Read, *J. Chem. Soc.*, 1935, 1138.
[10] A. F. Thomas, B. Willhalm, and J. H. Bowie, *J. Chem. Soc.* (*B*), 1967, 392; R. Pummerer, F. Aldebert, and H. Sperber, *Annalen*, 1953, **583**, 191.

H, 11.8%; M, 154). Purification of this mixture by preparative g.l.c. on Apiezon L (149°; 180 ml min^{-1} N$_2$) gave ($\pm$)-5-ethyl-*trans*-2,5-dimethylcyclohexanone (t_R 34.9 min) (Found: C, 77.9; H, 11.8%; M^+, 154. Calc. for C$_{10}$H$_{18}$O: C, 77.9; H, 11.8%; M, 154), $\nu_{max.}$ (film) 1 080, 1 220, 1 380, 1 460, 1 705, 2 050, 2 870, 2 920, and 2 970 cm^{-1}, τ 7.70 (1H, sextet, J 6.2 Hz), 7.80 (2 H), 8.00—8.50 (6 H, m), 8.97 (3 H, d, J 6.5 Hz), 9.02 (3 H, s), and 9.19 (3 H, t, J 5.5 Hz). The semicarbazone formed needles, m.p. 176—178°, identical with a previously prepared specimen [2] (from ethanol) (Found: C, 62.0; H, 9.8; N, 20.2. Calc. for C$_{11}$H$_{21}$N$_3$O: C, 62.5; H, 10.0; N, 19.9%). The 2,4-dinitrophenylhydrazone formed orange plates, m.p. 155—156°, identical with the previous specimen [2] (from ethanol) (Found: C, 57.6; H, 6.6; N, 16.6. Calc. for C$_{16}$H$_{22}$N$_4$O$_4$: C, 57.5; H, 6.6; N, 16.8%).

The isomeric ($\pm$)-5-*ethyl*-cis-2,5-*dimethylcyclohexanone* had t_R 36.6 min (Found: C, 77.9; H, 11.8%; M^+, 154), $\nu_{max.}$ (film) 720, 1 075, 1 210, 1 375, 1 455, 1 710, 2 850, 2 870, 2 925, and 2 960 cm^{-1}, τ 7.69 (1 H, sextet, J 6.2 Hz), 7.85 (2 H), 8.00—8.50 (6 H, m), 8.97 (3 H, d, J 6.5 Hz), 9.13 (3 H, t, J 6.5 Hz), and 9.15 (3 H, s). The *semicarbazone* formed needles, m.p. 185—187° (from ethanol) identical with the previous [2] specimen (Found: C, 62.1; H, 9.9; N, 20.2%).

Method B. Prepared from ($\pm$)-3-ethyl-3-methylcyclohexanone, ($\pm$)-2-hydroxymethylene-5-ethyl-5-methylcyclohexanone had b.p. 109° at 13 mmHg (lit.,[10] 127° at 20 mmHg) (Found: C, 71.1; H, 9.4. Calc. for C$_{10}$H$_{16}$O$_2$: C, 71.4; H, 9.6%). The p-*nitro-anil* formed stout, pale yellow prisms, m.p. 191° (from ethanol) (Found: C, 66.7; H, 6.6; N, 9.9. C$_{16}$H$_{20}$N$_2$O$_3$ requires C, 66.6; H, 7.0; N, 9.7%).

A solution of ($\pm$)-2-hydroxymethylene-5-ethyl-5-methylcyclohexanone (14.6 g) in benzene (150 ml) containing butane-1-thiol (9.1 g) and toluene-*p*-sulphonic acid (0.05 g) was refluxed for 24 h, with continuous removal of water, under nitrogen. Purified by distillation, ($\pm$)-2-n-*butylthiomethylene*-5-*ethyl*-5-*methylcyclohexanone* formed an oil (12.4 g), b.p. 134° at 0.1 mmHg (Found: C, 70.2; H, 10.1; S, 12.9. C$_{14}$H$_{24}$OS requires C, 70.0; H, 10.0; S, 13.3%). G.l.c. on Apiezon L (161°; 180 ml min^{-1} N$_2$) showed only one component, t_R 53.3 min.

A solution of this derivative (12.3 g) in ethanol (275 ml) containing W2 Raney nickel (80 g) was stirred at 60 °C during 1 h. After purification by distillation the crude product (which contained small quantities of cyclohexanols) was oxidised with Jones reagent and the resultant material purified by further distillation and then by preparative chromatography to yield ($\pm$)-5-ethyl-*trans*- and ($\pm$)-5-ethyl-*cis*-2,5-dimethylcyclohexanones, identical (t.l.c., g.l.c., and n.m.r., i.r., u.v., and mass spectra) with the products obtained by Method A.

Method C. 3,6-Dimethylcyclohex-2-enone, prepared by the literature [11] method, had b.p. 82° at 10 mmHg (lit.,[11] 95—100° at 22 mmHg) (Found: C, 77.7; H, 9.98; M^+, 124. Calc. for C$_8$H$_{12}$O: C, 77.4; H, 9.7%; M, 124). G.l.c. on Apiezon L (161°; 180 ml min^{-1} N$_2$) showed only one component, t_R 27.5 min. T.l.c. on silica showed only one spot, R_F 0.80, in benzene–ethyl acetate (4 : 1).

The 2,4-dinitrophenylhydrazone [12] formed red needles, m.p. 130—132° (from ethanol) (Found: C, 55.0; H, 5.5; N, 18.1. Calc. for C$_{14}$H$_{16}$N$_4$O$_4$: C, 55.3; H, 5.3; N, 18.4%), homogeneous by t.l.c. on silica (R_F 0.57 in benzene).

Ethylation of 3,6-dimethylcyclohex-2-enone (8.8 g) in ether (20 ml) by lithium diethylcuprate (as in Method B) gave a mixture (8.5 g) of ($\pm$)-5-ethyl-*trans*- and ($\pm$)-5-ethyl-

cis-2,5-dimethylcyclohexanone, identical with the products from Methods A and B.

Reduction of ($\pm$)-*5-Ethyl*-trans-*and* ($\pm$)-*5-Ethyl*-cis-*2,5-dimethylcyclohexanones to the Corresponding Cyclohexanols.—Method A.* A solution (at 0 °C) of an equilibrium mixture of ($\pm$)-5-ethyl-*trans*- and ($\pm$)-5-ethyl-*cis*-2,5-dimethylcyclohexanones (7 g) in ether (20 ml) was added gradually to a suspension of lithium aluminium hydride (1 g) in ether (100 ml) at 0 °C. After 3 h further at 0 °C (with stirring) the product was isolated in the normal manner and purified by distillation to yield a mixture of cyclohexanols (7 g), b.p. 110° at 15 mmHg. T.l.c. on silica [benzene–ethyl acetate (9 : 1)] showed (spray with 2,7-dichlorofluorescein in ethanol) two spots of equal intensity, under u.v. light, R_F 0.43 and 0.50. G.l.c. on Apiezon L (157°; 170 ml min^{-1} N$_2$) showed one major peak (96%), t_R 50.5 min, together with a minor peak (4%), t_R 44.2 min. On Diglycerol (123°; 175 ml min^{-1} N$_2$) two peaks of almost equal intensity, t_R 7.2 and 8.6 min, were detected. N.m.r. showed τ 6.10 (CH·OH, axial alcohol) and 6.65 (CH·OH, equatorial alcohol) in the ratio 82 : 18.

This mixture (5 g) was separated on Apiezon L (146°; 230 ml min^{-1} N$_2$) to give a mixture (0.95 g) (t_R 50.5 min) of ($\pm$)-cis-5-ethyl-*trans*-2,*trans*-5-dimethylcyclohexanol (12) and ($\pm$)-*trans*-5-ethyl-*cis*-2,*cis*-5-dimethylcyclohexanol (11) (0.08 g) together with a minor component (0.08 g) (t_R 44.2 min) ($\pm$)-cis-5-ethyl-*cis*-2,*cis*-5-dimethylcyclohexanol (13). The n.m.r. spectrum of this major fraction confirmed the absence of equatorial alcohols (no signal at τ 6.65); similarly the minor component contained exclusively equatorial alcohols. The second stage of preparative g.l.c. was performed on Diglycerol (144°; 200 ml min^{-1} N$_2$). The mixture of (11) and (12) (total 0.95 g) gave ($\pm$)-trans-5-*ethyl*-cis-2,cis-5-*dimethylcyclohexanol* (11) (0.27 g), t_R 7.2 min [t_R 4.0 min on Apiezon L (161°; 180 ml min^{-1} N$_2$)] (Found: C, 76.6; H, 12.6. C$_{10}$H$_{20}$O requires C, 76.9; H, 12.9%); t.l.c. on silica [benzene–ethyl acetate (9 : 1)] R_F 0.50; τ 6.12 (1 H, d, J 3.5 and 5.5 Hz), 8.4—9.3 (15 H, m), and 9.04 (3 H, s). The ($\pm$)-*hydrogen* 3-*nitrophthalate* formed plates, m.p. 195—197° [from light petroleum (b.p. 60—80°)] (Found: C, 61.5; H, 6.8; N, 4.0. C$_{18}$H$_{23}$NO$_6$ requires C, 61.9; H, 6.6; N, 4.0%).

The second component of the mixture was ($\pm$)-cis-5-*ethyl*-trans-2,trans-5-*dimethylcyclohexanol* (12) (0.23 g), t_R 7.6 min [t_R 4.1 min on Apiezon L (161°; 180 ml min^{-1} N$_2$)] (Found: C, 76.8; H, 13.1%); t.l.c. on silica [benzene–ethyl acetate (9 : 1)] R_F 0.43; τ 6.08 (1 H, ddd, J 4, 6.2, and 7.7 Hz), 8.3—9.3 (15 H, m), and 9.13 (3 H, s). The ($\pm$)-*hydrogen* 3-*nitrophthalate* formed plates, m.p. 179—181° [from light petroleum (b.p. 60—80°)] (Found: C, 61.9; H, 6.6; N, 3.7%).

Further purification by g.l.c. of the accumulated mixture of equatorial cyclohexanols gave (i) ($\pm$)-cis-5-*ethyl*-cis-2,cis-5-*dimethylcyclohexanol* (13), having t_R 35.7 and 20.7 min, respectively on Apiezon L (161°; 180 ml min^{-1} N$_2$) and Diglycerol (112°; 125 ml min^{-1} N$_2$), respectively (Found: C, 76.9; H, 13.1%); t.l.c. on silica [benzene–ethyl acetate (9 : 1)] R_F 0.43; (ii) a very small quantity of ($\pm$)-*trans*-5-ethyl-*trans*-2,*trans*-5-dimethylcyclohexanol (14), t_R 38.5 on Apiezon L (161°; 180 ml min^{-1} N$_2$), t_R 21.7 min on Diglycerol (112°; 120 ml min^{-1} N$_2$); t.l.c. on silica [benzene–ethyl acetate (9 : 1)] R_F 0.43.

[11] J. Dreux, *Bull. Soc. chim. France*, 1954, 1443.
[12] G. Pyne, R. C. Banerjee, and D. Nasipuri, *J. Indian Chem. Soc.*, 1963, **40**, 199.

Oxidation of the alcohols (11)—(13) at 20 °C with the Sarrett reagent during 18 h yielded quantitatively the parent ketones.

Method B. A slurry of lithium aluminium hydride (0.06 g) in ether (5 ml) was added at 0 °C (with stirring) to a solution of aluminium trichloride (0.67 g) in ether (10 ml); 30 min later a solution of (4) and (5) (0.7 g) in ether (10 ml) was slowly added; the mixture was then refluxed during 2 h and the cyclohexanols, identical with those from Method A, were isolated in the same manner.

(±)-cis- *and* (±)-trans-3-*Ethyl-3-methylheptan-6-olide.*— The isomeric (±)-5-ethyl-*trans*- and (±)-5-ethyl-*cis*-2,5-dimethylcyclohexanones (0.6 g each) were oxidised quantitatively with peroxytrifluoroacetic acid to the corresponding ε-lactones.[2] The (±)-trans-ε-*lactone* was an oil, b.p. 110° at 0.1 mmHg (Found: C, 70.5; H, 10.6. $C_{10}H_{18}O_2$ requires C, 70.5; H, 10.7%). G.l.c. on Apiezon L (207°; 200 ml min⁻¹ N_2) established its purity (t_R 35.1 min). A single band was also obtained on Reoplex 400, and on Diglycerol. The lactone showed $\nu_{max.}$ (film) 1 050, 1 115, 1 270, 1725, 2 850, 2 870, 2 935, and 2 965 cm⁻¹, τ 5.58 (1 H, sextet, J 6.5 Hz), 7.31 and 7.49 (2 H, AB, J 13.5 Hz), 8.1—9.2 (9 H, m), 8.65 (3 H, d, J 6.5 Hz), and 9.03 (3 H, s).

The (±)-cis-ε-*lactone* was an oil, b.p. 112° at 0.1 mmHg (Found: C, 70.1; H, 10.7%). G.l.c. on Apiezon L (207°; 200 ml min⁻¹ N_2) established its homogeneity (t_R 37.6 min),

confirmed by g.l.c. on Reoplex 400 and Diglycerol. The lactone showed $\nu_{max.}$ (film) 1 058, 1 110, 1 280, 1 721, 2 850, 2 870, 2 935, and 2 965 cm⁻¹, τ 5.58 (1 H, sextet, J 6.5 Hz), 7.66 and 7.64 (2 H, AB, J 13.5 Hz), 7.9—9.2 (9 H, m), 8.65 (3 H, d, J 6.5 Hz), and 9.02 (3 H, s).

(±)-*Methyl* 3-*Ethyl-6-hydroxy-4-methylheptanoate.*—Prepared as previously,[2] in quantitative yield from the *cis*-ε-lactone (0.4 g) and from the *trans*-ε-lactone (0.4 g), (±)-methyl 3-ethyl-6-hydroxy-3-methylheptanoate was an oil, b.p. 135° at 3.0 mmHg (Found: C, 75.6; H, 10.8. Calc. for $C_{11}H_{22}O_3$: C, 65.3; H, 11.0%). G.l.c. on Apiezon L (227°; 200 ml min⁻¹ N_2) and Diglycerol (112°; 220 ml min⁻¹ N_2) showed a single component, t_R 55.9 and 86.0 min, respectively. Samples of ester from each lactone exhibited identical behaviour, separately or in admixture.

Oxidation of this methyl ester gave (quantitatively) (±)-methyl 3-ethyl-3-methyl-6-oxoheptanoate,[2] b.p. 119° at 1 mmHg (Found: C, 66.2; H, 10.3. Calc. for $C_{11}H_{20}O_3$: C, 66.0; H, 10.1%). G.l.c. on Apiezon L (227°; 200 ml min⁻¹ N_2) showed one component, t_R 22.9 min.