Oxidative Displacement of Hypervalent Iodine from Alkyl Iodides

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Oxidative displacement of iodine from primary alkyl iodides and *vic*-substituted iodocyclohexanes with *m*-chloroperbenzoic acid in either dichloromethane or t-butyl alcohol–water gives primary alcohols and *vic*-substituted cyclohexanols, respectively. Retention of configuration at the displacement centre occurs for all of the *trans-vic*-substituted iodocyclohexanes except the iodoacetate and iodotrifluoroacetate where inversion of configuration occurs to give *cis*-hydroxy-esters. Oxidation of (*S*)-2-iodo-octane occurs with almost complete inversion to give (*R*)-octan-2-ol but also affords octan-1-ol, octan-3-ol, and octan-2-one.

ALTHOUGH alkyl iodides can be oxidised by electrochemical methods,[1] they are normally inert to the more common oxidising agents such as ozone, periodate, and hydrogen peroxide.[2] From the premise that iodine in a higher oxidation state would provide a better leaving group than univalent iodine, we have found that primary alkyl iodides and substituted iodocyclohexanes are readily converted into alcohols by oxidative displacement with *m*-chloroperbenzoic acid.[3] A similar finding for primary iodides has been reported recently by Reich

and Peake,[2] who suggested that the oxidation gives an iodoso-compound which rearranges to a hypoiodite which in turn is converted into the alcohol under the reaction conditions [equation (1)].

(1) $R^1 = I, R^2 = H, R^3 = O \cdot CO \cdot CH_3$
(2) $R^1 = I, R^2 = H, R^3 = O \cdot CO \cdot CF_3$
(3) $R^1 = I, R^2 = H, R^3 = N_3$
(4) $R^1 = I, R^2 = H, R^3 = OMe$
(5) $R^1 = I, R^2 = H, R^3 = OH$
(6) $R^1 = I, R^2 = H, R^3 = Br$
(7) $R^1 = I, R^2 = H, R^3 = Cl$
(8) $R^1 = I, R^2 = H, R^3 = NCS$
(9) $R^1 = H, R^2 = OH, R^3 = O \cdot CO \cdot CH_3$
(10) $R^1 = H, R^2 = OH, R^3 = O \cdot CO \cdot CF_3$
(11) $R^1 = H, R^2 = R^3 = O \cdot CO \cdot CF_3$
(12) $R^1 = H, R^2 = R^3 = OH$
(13) $R^1 = OH, R^2 = H, R^3 = N_3$
(14) $R^1 = OH, R^2 = H, R^3 = OMe$
(15) $R^1 = O \cdot CO \cdot m - ClC_6H_4, R^2 = H, R^3 = OMe$
(16) $R^1 = OH, R^2 = H, R^3 = Br$
(17) $R^1 = OH, R^2 = H, R^3 = Cl$
(18) $R^1 = R^3 = OH, R^2 = H$

(19) $R^1 = I, R^2 = SCN$
(20) $R^1 = SCN, R^2 = I$
(21) $R^1 = OH, R^2 = SCN$
(22) $R^1 = SCN, R^2 = OH$
(23) $R^1 = O \cdot CO \cdot m - ClC_6H_4, R^2 = SCN$
(24) $R^1 = SCN, R^2 = O \cdot CO \cdot m - ClC_6H_4$
(25) $R^1 = I, R^2 = NCS$
(26) $R^1 = NCS, R^2 = I$

(27)

(28) R = I
(29) R = OH

(30) β−epoxide
(31) α−epoxide

$Me \left[CH_2 \right]_7 R$
(32) R = I
(33) R = OH
(34) $R = O \cdot CO \cdot m - ClC_6H_4$

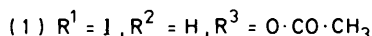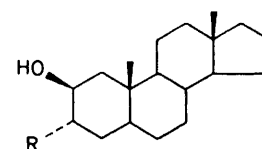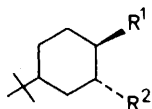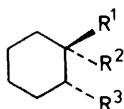$Me \left[CH_2 \right]_3 R$
(35) R = I
(36) R = OH

$Me \left[CH_2 \right]_4 R$
(37) R = I
(38) R = OH

$Me \left[CH_2 \right]_5 CH(R)Me$
(39) R = I
(40) R = OH
(41) $R = O \cdot CO \cdot m - ClC_6H_4$

$Me \left[CH_2 \right]_5 Ac$
(42)

Our initial reactions were carried out with a series of *trans-vic*-substituted iodocyclohexanes using 2.2 mol equiv. of *m*-chloroperbenzoic acid in dichloromethane (Table 1). This afforded high to moderate yields of the corresponding vicinal alcohols but varying amounts of *trans-vic*-substituted *m*-chlorobenzoate esters were also

$$RI \rightleftharpoons RI\colon O \longrightarrow [R^+IO^- \longleftrightarrow R^\cdot IO^\cdot] \longrightarrow ROI \longrightarrow ROH \qquad (1)$$

formed, depending on the nature of the neighbouring group. In a control experiment it was shown that these latter products did not arise by simple esterification of the alcohol with *m*-chlorobenzoic acid produced in the reaction, since treatment of octan-2-ol with *m*-chlorobenzoic acid resulted in a quantitative recovery of starting material. Treatment of the iodohydrin (5) with *m*-chloroperbenzoic acid in di-deuteriodichloromethane

TABLE 1

Reactions of iodides with *m*-chloroperbenzoic acid in dichloromethane

Compound	*m*-chlorobenzoic acid (mol equiv.)	Reaction time (min)	Products	Yield (%)
(1) [a,b]	2.2	60	(9) [a]	95
(2) [a]	2.2	180	(10) [c]	100
(3) [d]	3.0	5	(13) [e]	77
(4) [a]	2.2	5	(14) [f]	31 [g]
			(15)	8 [g]
(19) (20) [h]	4.5	5	(21) (22) [h,i]	34 [g]
			(23) (24) [h]	12 [g]
(5) [a]	2.2	5	(27) [a,j]	100 [k]
(28) [l]	2.2	5	(30) [l]	100 [k]
(32)	2.2	1	(33)	95
(35)	2.2	5	(36)	100 [k]
(37)	2.2	5	(38)	100 [k]
(39) [m]	2.2	10	(40)	56 [k,n]
			(41)	29 [k,o]
			(42)	9 [k]
			(33)	6 [k]

[a] R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J.C.S. Perkin I*, 1974, 1858. [b] Ref. 17. [c] Reduction with LiAlH₄ in ether for 2 h gave *cis*-cyclohexane-1,2-diol (12) (S. Winstein and R. E. Buckles, *J. Amer. Chem. Soc.*, 1942, **64**, 2780; S. Winstein, *ibid.*, p. 2792; S. Winstein, H. V. Hess, and R. E. Buckles, *ibid.*, p. 2796). [d] Ref. 9. [e] C. A. Van der Werf, R. Y. Heisler, and W. E. McEwan, *J. Amer. Chem. Soc.*, 1954, **76**, 1231; R. C. Cambie, R. C. Hayward, P. S. Rutledge, T. Smith-Palmer, and P. D. Woodgate, *J.C.S. Perkin I*, 1976, 840. [f] Ref. 22. [g] Isolated by preparative t.l.c. [h] 5 : 4 mixture. [i] Identified by comparison with an authentic mixture (see Experimental section). [j] M. S. Newman and C. A. Vander-Werf, *J. Amer. Chem. Soc.*, 1945, **67**, 233. [k] Estimated from ¹H n.m.r. analysis. [l] Ref. 4. [m] Racemate. [n] Contained some octan-3-ol. [o] Contained a trace of 1-ethylhexyl *m*-chlorobenzoate.

in a ¹H n.m.r. tube showed rapid and exclusive formation of the epoxide (27) rather than of a *vic*-diol. Similarly, 3α-iodo-5α-androstan-2β-ol (28) gave the β-epoxide (30),[4] an authentic sample of which was prepared in 98% yield by treatment of 5α-androst-2-ene with mercuric oxide and iodine.[5] Although ¹H n.m.r. analysis showed the immediate loss of the CHI resonance from both *trans*-1-azido-2-iodocyclohexane (3) and the iodocyclohexyl ether (4), it was necessary in these cases to determine the product composition after work-up and isolation owing to the superimposition of downfield signals in the spectra. Oxidative displacement of iodine from 1-iodo-octane proceeded smoothly in dichloromethane, while the secondary halide, iodocyclohexane, rapidly gave 1,2-epoxycyclohexane (27) in quantitative yield with 2.2 mol equiv. of peracid. With only 1 equiv. of oxidant the latter substrate gave (¹H n.m.r. analysis) a mixture of starting material, epoxide (27), and unidentified compounds. No cyclohexene was detected, although the pathway for formation of the epoxide

presumably involves conversion into trivalent iodine and elimination *via* a cationic intermediate to the alkene which must then react rapidly with the peracid.[2] In accord with this result, treatment of the allylic iodide 3-iodo-1-t-butylcyclohexene with *m*-chloroperbenzoic acid failed to result in selective oxidation at either functional group and a mixture of unidentified products was obtained. Oxidation of the chiral secondary halide (S)-(+)-2-iodo-octane,[6,7] which was shown (¹H n.m.r.) to be free of contamination by 1-iodo-octane, gave a mixture containing (R)-(−)-octan-2-ol (40),[8] its *m*-chlorobenzoate ester (41), octan-2-one (42), and a trace of octan-1-ol. Since attempted isolation of the components of the mixture by preparative g.l.c. resulted in only low recovery of the products, it was expedient to employ an alternative, albeit less direct, procedure involving distillation from the crude oxidation product of a fraction containing octan-1-ol, octan-2-ol, and octan-2-one. Treatment of this fraction with lithium di-isopropylamide–*m*-chlorobenzoyl chloride effected rapid esterification and allowed the easy separation (preparative t.l.c.) and identification (¹H n.m.r.) not only of 1-methylheptyl *m*-chlorobenzoate (41), but also of octyl *m*-chlorobenzoate (34) admixed with the enol form of the 1,3-diketone resulting from reaction of the enolate of octan-2-one with the acyl chloride. A pure sample of each of the *m*-chlorobenzoates (34) and (41) for spectral comparison was obtained by similar esterification of a commercial sample of chiral (R)-(−)-octan-2-ol (which contained a trace of octan-1-ol), followed by preparative t.l.c.

In an attempt to prevent formation of the *m*-chlorobenzoate ester, reactions were also carried out in a

(43) (44) (45)

(46) (47)
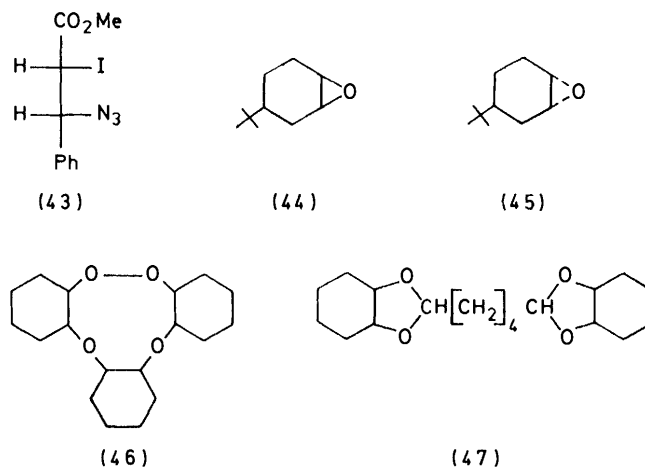
mixture of t-butyl alcohol and water. Despite the fact that reactions were somewhat slower and in some cases a higher molar ratio of *m*-chloroperbenzoic acid to substrate was used, cleaner conversions to the desired alcohols were now achieved (Table 2). A control experiment using the iodoazide (3) in t-butyl alcohol–water, but omitting the peracid, gave a 91% recovery of starting material. No reaction occurred with the secondary iodide, methyl *erythro*-3-azido-2-iodo-3-

phenylpropanoate (43),[9] which bears a strong electron-withdrawing methoxycarbonyl group at the α-carbon, and m-chloroperbenzoic acid (3 mol equiv.) in dichloromethane for 24 h or in t-butyl alcohol–water with m-chloroperbenzoic acid (5 mol equiv.) for 5 days.

<div align="center">TABLE 2</div>

Reactions of iodides with m-chloroperbenzoic acid in t-butyl alcohol–water (3 : 1)

Compound	m-chloro-perbenzoic acid (mol. equiv.)	Reaction time (min)	Products	Isolated yield (%)
(1) [a,b]	3	15	(9) [a]	78
(3) [c]	4	10	(13) [d]	84
(4) [a]	3	30	(14) [e]	67
(5) [a]	3	25	(18) [f]	45 [g]
(6) [h]	3	7	(16) [i]	74
(7) [j]	4	60	(17) [k] (27)	[l]
(19) (20) [m]	10	60	(21) (22) [m]	77
(28) [n]	3	15	{ (29)	49
			(30)	49
(39) [o]	2.2	10	{ (40)	53
			(42)	4

[a] Table 1, footnote [a]. [b] Ref. 17. [c] Ref. 9. [d] Table 1, footnote [e]. [e] Ref. 22. [f] References in Table 1, footnote [c]. [g] The low yield was due to the high solubility of the product in water. [h] T. Torgrimsen and P. Klaeboe, Acta Chem. Scand., 1971, 25, 1915. [i] G. Bodennec, H. Bodot, and A. Nattaghe, Bull. Soc. chim. France, 1967, 876. [j] R. C. Cambie, W. I. Noall, G. J. Potter, P. S. Rutledge, and P. D. Woodgate, J.C.S. Perkin I, 1977, 26. [k] H. Bodot, D. Dan Dicko, and Y. Gounelle, Bull. Soc. chim. France, 1967, 870. [l] Mixture of (17) and (27) (4 : 1) and unidentified material. [m] Mixture in the ratio 5 : 4. [n] Ref. 4. [o] Ref. 6.

Although thiocyanates are known to undergo oxidation with m-chloroperbenzoic acid to give the corresponding sulphinyl cyanides and then sulphonyl cyanides [10] [equation (2)], only low yields of the sul-

$$RSCN \longrightarrow R{\cdot}SO{\cdot}CN \longrightarrow R{\cdot}SO_2{\cdot}CN \qquad (2)$$
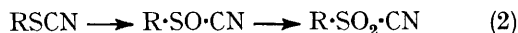
phonyl derivatives are obtained from simple alkyl thiocyanates even under vigorous conditions.[11] In the present work, treatment of a mixture of the regioisomeric iodothiocyanates (19) and (20) with 2.2 mol equiv. of m-chloroperbenzoic acid resulted in only partial disappearance of the CHI signal in the [1]H n.m.r. spectrum. Further reaction in either dichloromethane or t-butyl alcohol–water with increased molar ratios of the peracid to substrate gave predominantly the thiocyanatohydrins (21) and (22) with no detectable sign of oxidation of the thiocyanate group. The assignment of structures (21) and (22) was confirmed by spectral comparison with an authentic mixture of these isomers prepared by cleavage of a mixture of the stereoisomeric 4-t-butylcyclohexane epoxides (44) and (45) with thiocyanic acid.[12] Treatment of the iodoisothiocyanate (8) with m-chloroperbenzoic acid (2.2 mol equiv.) in dichloromethane for 10 min gave no reaction but with additional peracid (2.2 mol equiv.) no starting material remained after 2 h. However, while work-up and [1]H n.m.r. and i.r. spectral analysis indicated the presence of m-chlorobenzoate ester, hydroxy-, and possibly isocyanato-groups, no pure product could be isolated. Inconclusive results were also obtained with

the iodoisothiocyanate (8) using 6 mol equiv. of m-chloroperbenzoic acid in t-butyl alcohol–water, and with a regioisomeric mixture (ca. 4 : 5) of the iodoisothiocyanates (25) and (26) in the same solvent. We conclude that reaction of iodoisothiocyanates with m-chloroperbenzoic acid is less selective than that of iodothiocyanates and that the mixtures of products from the former compounds arise by oxidation at more than one site in the molecule (cf. ref. 13).

With the exception of the iodo-esters (1) and (2), all of the trans-vic-substituted iodocyclohexanes examined during the present study gave alcohols and m-chlorobenzoate esters with retention of configuration as a result of neighbouring group participation (Scheme 1).
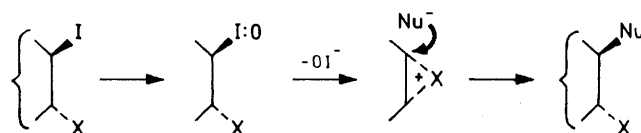
<div align="center">SCHEME 1</div>

Formation of the cis-hydroxy-esters (9) and (10) from the trans-iodoacetate (1) and trans-iodotrifluoroacetate (2), respectively, is an exception wherein the stereochemistry of the products is determined by attack of OI[−] or of water at C-2 of a 2-alkyl-1,3-dioxolan-2-ylium ion. In the latter case, the intermediate would be the same as that which gives rise to products of cis-stereochemistry in the Woodward–Prévost reaction (Scheme 2).[14] The retention of configuration observed for the
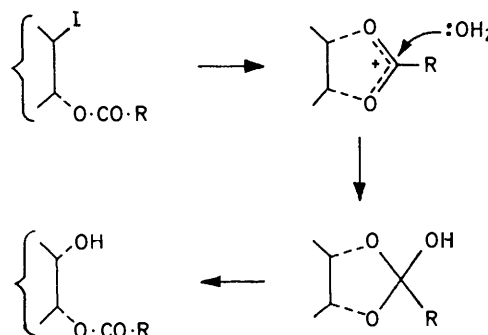
<div align="center">SCHEME 2</div>

trans-vic-substituted iodocyclohexanes parallels the recent work of Zbiral and his co-workers [15] who have shown that a neighbouring group effect operates during the solvolysis of vic-iodoazides and vic-iodobromides, etc., with iodine(III) trifluoroacetate. However, solvolysis of a vic-iodotrifluoroacetate with iodine(III) trifluoroacetate has been shown by Buddrus,[16] and confirmed by us, to proceed with complete inversion of configuration at the carbon bearing the iodo-group, a result similar to that observed in the present work with the iodo-esters (1) and (2).

The chiral products isolated from the reaction of (S)-(+)-2-iodo-octane with m-chloroperbenzoic acid in dichloromethane showed almost complete inversion of

configuration. Thus, in this case where reaction cannot involve neighbouring group participation, the major reaction pathway must involve an S_N2 mechanism (cf. ref. 2). However, the isolation of a low yield of octyl m-chlorobenzoate (34) from the mixture suggests the involvement also of carbo-cationic intermediates. On this basis some octan-3-ol and its m-chlorobenzoate ester would be expected also.[2] Although no 1-ethyl-hexyl m-chlorobenzoate was identified, the experimental procedure used to isolate chemically pure chiral 1-methylheptyl m-chlorobenzoate may have resulted in non-recovery of the former compound.

On the assumption that oxidative displacement of iodine occurs through the intermediacy of a hypervalent, presumably trivalent, iodo-compound, an attempt was made to form an I_2O species [17,18] by reaction of equiv-alent amounts of m-chloroperbenzoic acid and molecular iodine in dichloromethane at room temperature for 5 min. However, no colour change was observed and addition of 5α-androst-2-ene to this mixture gave neither the iodohydrin (28) nor the β-epoxide (30) but a quanti-tative yield of the α-epoxide (31),[4] the product expected from direct attack of the peracid on the less hindered face of the molecule.

Solvent incorporation occurred when the oxidations were carried out in methanol or acetic acid. Thus, treatment of 1-iodo-octane with m-chloroperbenzoic acid in methanol gave 1-methoxyoctane in 91% yield while similar treatment of 2-iodo-octane gave 2-methoxy-octane as the major product in addition to octan-2-one. Oxidation of 1-iodo-octane in acetic acid gave octyl acetate (72%), octan-1-ol (24%), and starting material (4%) while similar oxidation of 2-iodo-octane gave 1-methylheptyl acetate (84%) and octan-2-one (15%).

In earlier work attempts were made to oxidise alkyl iodides with reagents other than m-chloroperbenzoic acid. However, no reaction occurred with t-butyl hydroperoxide or with N-chlorosuccinimide in dichloro-methane or with sodium hypochlorite and tetrabutyl-ammonium hydrogensulphate in chloroform-water. Little reaction occurred when the trans-iodotrifluoro-acetate (2) was treated with 1 mol equiv. of trifluoro-peracetic acid in dichloromethane and even with 10 mol equiv. of the peracid, the product contained (^1H n.m.r. analysis) ca. 50% of starting material. However, the product also contained the cis-bis(trifluoroacetate) (11) together with the hydroxytrifluoroacetate (10) and the corresponding diol (12) resulting from cleavage of the trifluoroacetate ester during work-up. Use of 2.4 mol equiv. of the peracid in a mixture of trifluoroacetic anhydride and dichloromethane resulted in complete conversion of the iodotrifluoroacetate (2) into a mixture of the cis-bis(trifluoroacetate) (11) and its monohydroxy-analogue (10). In order to circumvent the problem of ester hydrolysis during work-up, the iodotrifluoroacetate was treated with the peracid and trifluoroacetic acid at 20 °C for 3 h and the crude product [containing 95% of one compound (g.l.c. analysis)] reduced directly with lithium aluminium hydride. This sequence afforded

cis-cyclohexane-1,2-diol (12) * in an overall yield of 90%.

Ogata and Aoki [20] have shown that the oxidation of iodocyclohexane with peracetic acid in acetic acid gives a mixture of an acetate, a vic-diacetate, and a vic-iodoacetate, while Zbiral and Linkeseder [21] have shown that iodoalkanes are oxidised by iodine(III) trifluoro-acetate in ether to 2-iodoalkyl trifluoroacetates. In dichloromethane the latter reaction proceeds by replace-ment of the halogen to give the vic-bis(trifluoroacetate). Simple substitution, for example of 1-iodo-octane to form octyl trifluoroacetate and octyl ethyl ether, occurred in only low yield. The oxidation of alkyl iodides to alcohols or alcohol derivatives with m-chloroperbenzoic acid reported above not only provides a complementary method to Zbiral's reaction, but also indicates the necessity for careful choice of oxidant in e.g. epoxidation or Baeyer-Villiger reactions when the substrate also contains iodine.

EXPERIMENTAL

General experimental details are given in ref. 17. Optical rotations were measured for solutions in $CHCl_3$ with a Perkin-Elmer 241 polarimeter. Preparative g.l.c. was carried out with a Varian Aerograph series 1800 instrument on an aluminium column (2.5 m × 1 cm) packed with 5% OV-17 on Chromosorb W-HP at 100 °C and at 250 °C for less volatile material. The carrier gas was N_2 and fractions were collected in a glass coil at −78 °C.

General Procedures for Oxidative Displacement.—(a) In dichloromethane. A mixture of the iodide (1—5 mmol) and 85% m-chloroperbenzoic acid in dichloromethane (5—25 ml) was stirred at 20 °C for the recorded time (Table 1). The mixture was then poured into water and extracted with dichloromethane. The extract was washed succes-sively with water, saturated aqueous sodium hydrogen-sulphite, and saturated aqueous sodium hydrogencarbonate, and the solvent was removed from the dried ($MgSO_4$) solu-tion under reduced pressure. Mixtures of products were normally separated by preparative t.l.c. with hexane–chloroform (2 : 1 or 1 : 1).

(b) In t-butyl alcohol–water (3 : 1). A mixture of the iodide (1—2 mmol) and m-chloroperbenzoic acid in t-butyl alcohol–water (3 : 1) (20 ml) was stirred at 20 °C for the recorded time (Table 2). Solvent was removed from the mixture under reduced pressure and the residue was extracted with dichloromethane. The extract was then worked up as in (a).

The results are summarised in Tables 1 and 2; products not identified by comparison with authentic samples are described below.

trans-2-Methoxycyclohexanol (14) had b.p. 70° at 0.5 mmHg (lit.,[22] 107—111° at 65 mmHg), $v_{max.}$ 3 500 (OH) and 1 095 cm^{-1} (CO), δ 1.46 (m, CH_2), 2.85 (m, CHOH), 3.27 (m, CHOMe), 3.32 (s, OMe), and 3.62br (s, OH, exchanged with D_2O), m/e 130 (M^+).

trans-2-Methoxycyclohexyl m-chlorobenzoate (15) was obtained as a viscous oil, $v_{max.}$ 1 725 (ester CO) and 1 259 cm^{-1} (OCOAr), δ 1.64 (m, CH_2), 3.25 (m, CHOMe), 3.34 (s, OMe), 4.89 (m, $W_{\frac{1}{2}}$ 11.5 Hz, CHOCOAr), and 7.57 (m, ArH), m/e 268 (M^+) and 236 (M^+ − MeOH).

*A compound from the action of iodine(I) acetate on cis-cyclohexane-1,2-diol which was tentatively identified as the peroxide (46) [19] has now been identified as the bisacetal of hexane-1,6-dial with cis-cyclohexane-1,2-diol, i.e. (47).

The mixture of c-4-t-butyl-t-2-thiocyanatocyclohexan-r-1-yl m-chlorobenzoate (23) and t-3-t-butyl-t-6-thiocyanato-cyclohexan-r-1-yl m-chlorobenzoate (24) was an oil, $v_{max.}$ 2 155 (SCN), 1 725 (ester CO), and 1 250 cm^{-1} (OCOAr), δ 1.19 (m, CH$_2$ and CH), 0.92 and 0.95 (2s, CMe$_3$), 3.94 (m, $W_{\frac{1}{2}}$ 13.5 Hz, CHSCN), 5.29 (m, $W_{\frac{1}{2}}$ 14 Hz, CHOCOAr), and 7.65 (m, ArH), m/e (no $M^{+\cdot}$), 195 ($M^{+\cdot}$ − m-CBA), and 139 ($M^{+\cdot}$ − m-CBA − C$_4$H$_8$).

Reaction of 4-t-Butylcyclohexene with Iodine and Potassium Thiocyanate.—A mixture of 4-t-butylcyclohexene (1.0 g, 7.2 mmol), iodine (4.4 g, 17.3 mmol), and potassium thiocyanate (2.1 g, 26.1 mmol) in chloroform (30 ml) was stirred in the dark at 20 °C for 20 h. Work-up [23] yielded an oil (2.12 g) which after preparative t.l.c. (hexane–chloroform, 9 : 1) gave (i) a regioisomeric mixture (5 : 4) of c-4-iodo-t-3-isothiocyanato-r-1-t-butylcyclohexene (25) and t-3-iodo-c-4-isothiocyanato-r-1-t-butylcyclohexane (26) (0.13 g, 12%), $v_{max.}$ 2 042 cm^{-1} (NCS), δ 0.93 (s, CMe$_3$), 1.79 (m, CH$_2$,CH), 4.02, 4.23 (2m, $W_{\frac{1}{2}}$ 5 and 5 Hz, CHNCS), and 4.67 (m, $W_{\frac{1}{2}}$ 12 Hz, CHI), and (ii) a regiosomeric mixture (5 : 4) of c-4-iodo-t-3-thiocyanato-r-1-t-butylcyclo-hexane (19) and t-3-iodo-c-4-thiocyanato-r-1-t-butylcyclo-hexane (20) (0.69 g, 65%), $v_{max.}$ 2 160 cm^{-1} (SCN), δ 0.92 (s, CMe$_3$), 1.71 (m, CH$_2$,CH), 4.19 (m $W_{\frac{1}{2}}$ 11 Hz, CHSCN), and 4.96 (m, $W_{\frac{1}{2}}$ 13 Hz, CHI).

c-4-t-*Butyl*-t-2-*thiocyanatocyclohexan*-r-1-*ol* (21) *and* t-3-t-*butyl*-t-6-*thiocyanatocyclohexan*-r-1-*ol* (22).—A mixture of 4-t-butylcyclohexene (0.18 g, 1.28 mmol) and m-chloroper-benzoic acid (0.30 g, 1.47 mmol) in dichloromethane (5 ml) was stirred at 20 °C for 1 h. The mixture was filtered, the filtrate diluted with dichloromethane, and the solution washed with aqueous sodium disulphite and saturated aqueous sodium hydrogencarbonate. Removal of solvent from the dried solution gave a mixture (0.17 g, 88%) of the epimers 3β,4β-epoxy-1-t-butylcyclohexane (44) and 3α,4α-epoxy-1-t-butylcyclohexane (45) (ca. 1 : 1), δ 0.82 (s, CMe$_3$), 1.63 (m, CH$_2$ and CH), and 3.02 and 3.07 (m, $W_{\frac{1}{2}}$ 7.5 Hz, 3,4-H), m/e 154 (M^+), 139 ($M^{+\cdot}$ − Me), 97 ($M^{+\cdot}$ − CMe$_3$), 81 (C$_6$H$_9$$^+$), and 57 (CMe$_3$$^+$).

A solution of the epoxides (44) and (45) in ether (1 ml) was treated with an ethereal solution of thiocyanic acid [prepared by the addition of 85% phosphoric acid (1.67 g, 17.1 mmol) in portions with shaking to potassium thio-cyanate (1.11 g, 11.4 mmol) dissolved in ice–water and ether] and the mixture was stirred at 20 °C for 25 min. The mixture was diluted with ether and washed with saturated aqueous sodium hydrogencarbonate. Removal of solvent from the dried solution gave a mixture (ca. 1 : 1) of c-4-t-butyl-t-2-thiocyanatocylohexan-r-1-ol (21) and 5-t-butyl-t-3-t-butyl-t-6-thiocyanatocyclohexan-r-1-ol (22) (92 mg, 76%), b.p. 133° at 0.7 mmHg, $v_{max.}$ 3 455 (OH) and 2 155 cm^{-1} (SCN), δ 0.86 (s, CMe$_3$), 1.57 (m, CH$_2$,CH), 3.64 (m, $W_{\frac{1}{2}}$ 11 Hz, CHOH), 4.01 (m, $W_{\frac{1}{2}}$ 12 Hz, CHSCN),[12] and 4.32br (s, OH, exchanged with D$_2$O), m/e 213 ($M^{+\cdot}$), 212 ($M^{+\cdot}$ − H), 198 ($M^{+\cdot}$ − Me), and 170 ($M^{+\cdot}$ − HOCN).

Reaction of (S)-(+)-2-*Iodo-octane with* m-*Chloroperbenzoic Acid.*—(S)-(+)-2-Iodo-octane (1.25 g, 5.23 mmol) [from (R)-(−)-octan-2-ol, $[\alpha]_D$ −9.05°,[8] 91.4% optically pure, and phosphorus tri-iodide [7]], $[\alpha]_D^{21.5}$ + 46.65°,[6] 72.6% optically pure, and m-chloroperbenzoic acid (1.37 g, 6.8 mmol) were stirred in dichloromethane (25 ml) at 20 °C for 1 h. The crude product was distilled at 100 °C and 25 mmHg. A portion (0.16 g) composed mainly of (¹H n.m.r.) of octan-2-ol, with small amounts of octan-1-ol and octan-2-one, was redistilled. This fraction (0.11 g, 0.83 mmol) was dissolved

in tetrahydrofuran (2 ml) and added dropwise over 1 min at 0 °C to a solution of lithium di-isopropylamide (1.08 mmol) in tetrahydrofuran (5 ml). m-Chlorobenzoyl chlor-ide (0.16 g, 0.9 mmol) was added and the mixture was stirred for a further 5 min. Preparative t.l.c. (hexane, 2 elutions) of the crude product (0.18 g) followed by distill-ation gave (i) pure (g.l.c.) (R)-(−)-1-methylheptyl m-chloro-benzoate (80 mg), $[\alpha]_D^{22}$ −25.9°, 69.3% optically pure, b.p. 120° at 0.5 mmHg, and (ii) an inseparable mixture (15 mg, 3 : 5) of octyl m-chlorobenzoate and 1-(3-chlorophenyl)-1-hydroxynon-1-en-3-one, δ 2.36 (t, J 7 Hz, 4-H$_2$), 6.00 (s, 2-H), and 16.18br (OH, exchanged with D$_2$O).

In a separate experiment the (R)-(−)-1-methylheptyl m-chlorobenzoate, formed directly in the oxidation procedure, was isolated by usual work-up and preparative t.l.c. of the crude product. It had $[\alpha]_D$ −22.97°, 61.6% optically pure.

(R)-(−)-1-*Methylheptyl* m-*Chlorobenzoate* (41).—Butyl-lithium (1 ml, 1.6 mmol) was added dropwise over 1 min to a solution of di-isopropylamine (0.22 ml, 1.57 mmol) in tetrahydrofuran (5 ml) under argon at 0 °C. (R)-(−)-Octan-2-ol (0.25 ml, 1.5 mmol), $[\alpha]_D^{17}$ −9.05° (Aldrich Chemical Co. Ltd.) and m-chlorobenzoyl chloride (0.2 ml, 1.6 mmol) were then added to the stirred mixture at 0 °C. The mixture was stirred for 6 min, treated with water, and extracted with ether. The extract was washed successively with water, dilute hydrochloric acid, water, and saturated aqueous sodium hydrogencarbonate. Removal of the solvent from the dried solution gave an oil (0.53 g) which on repeated preparative t.l.c. (hexane) gave (i) (R)-(−)-1-*methylheptyl* m-*chlorobenzoate* (0.34 g, 81%), b.p. 120° at 0.5 mmHg, $[\alpha]_D^{22}$ −34.09° (Found: C, 67.2; H, 8.0; Cl, 13.4. C$_{15}$H$_{21}$ClO$_2$ requires C, 67.0; H, 8.1; Cl, 13.2%), $v_{max.}$ 1 720 (ester CO) and 1 260 cm^{-1} (OCOAr), δ 0.87 (distorted t, Me), 1.49 (m, CH$_2$), 1.32 (d, J 6 Hz, CH$_3$CHOCOAr), 5.12 (distorted sextet, $W_{\frac{1}{2}}$ 14.5 Hz, CHOCOAr), and 7.57 (m, ArH), m/e 268 ($M^{+\cdot}$), 156 (mCBA$^{+\cdot}$), and 139 (C$_8$H$_{17}$O$^+$), and (ii) octyl m-chlorobenzoate (5 mg, 1%), $v_{max.}$ 1 725 (ester CO) and 1 260 cm^{-1} (OCOAr), δ 1.00 (distorted t, Me), 1.53 (m, CH$_2$), 4.27 (t, J 6 Hz, CH$_2$OCOAr), and 7.53 (m, ArH), m/e (no $M^{+\cdot}$), 212 ($M^{+\cdot}$ − C$_4$H$_8$), 156 (mCBA$^{+\cdot}$), 139 (mClC$_6$H$_4$CO$^+$), and 111 (C$_6$H$_4$Cl$^+$).

Reaction of 2-*Iodo-octane with* m-*Chloroperbenzoic Acid.*—(a) *In methanol.* A mixture of 2-iodo-octane (0.32 g, 1.33 mmol), and m-chloroperbenzoic acid (0.59 g, 2.94 mmol) in anhydrous methanol (5 ml) was stirred at 20 °C for 1 h. The mixture was poured into aqueous sodium hydrogen-carbonate and extracted with pentane. The extract was washed successively with water, dilute hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and water. Removal of solvent from the dried solution gave a volatile oil (0.21 g) composed mainly of 2-methoxyoctane, and octan-2-one (3 : 1) (comparative g.l.c. and ¹H n.m.r. analysis). An authentic sample of 2-methoxyoctane was prepared by stirring octan-2-ol (0.41 g, 3.16 mmol) with 70% perchloric acid (0.67 g, 6.6 mmol) and trimethyl orthoformate [24] (5 ml) at 20 °C for 15 min. Work-up as above gave a volatile oil (0.16 g, 30%), δ 0.88 (distorted t, Me), 1.05 (d, J 6.5 Hz, CH$_3$CHOMe), 1.42 (m, CH$_2$), 3.17 (m, CHOMe), and 3.22 (s, OMe).

A similar oxidation of 1-iodo-octane gave 1-methoxy-octane (91%).

(b) *In acetic acid.* A mixture of 2-iodo-octane (0.20 g, 0.83 mmol) and m-chloroperbenzoic acid (0.38 g, 1.8 mmol) in acetic acid (20 ml) was stirred at 20 °C for 30 min.

Work-up as in the general procedure (a) gave an oily solid composed of 1-methylheptyl acetate (84%) and octan-2-one (15%).

A similar oxidation of 1-iodo-octane gave octyl acetate (72%), octan-1-ol (24%), and starting material (4%).

2β,3β-Epoxy-5α-androstane (30).—A mixture of 5α-androst-2-ene [25] (53 mg, 0.2 mmol), mercuric oxide (0.22 g, 1.02 mmol), and iodine (0.26 g, 1.02 mmol) in ether–water (25 : 1 v/v) (10 ml) was stirred in the dark at 20 °C for 64 h. The mixture was filtered and the filtrate was diluted with dichloromethane and washed with saturated aqueous sodium hydrogensulphite and then water. Removal of solvent from the dried solution gave an oil (0.24 g) which was dissolved in chloroform, re-filtered, and concentrated to give 2β,3β-epoxy-5α-androstane (55 mg, 98%) as a clear oil (correct ^{1}H n.m.r. spectrum [4]).

Reaction of trans-*2-Iodocyclohexyl Trifluoroacetate with Trifluoroperacetic Acid.*—(a) A mixture of *trans*-2-iodocyclohexyl trifluoroacetate (0.10 g, 0.31 mmol) and trifluoroperacetic acid [from trifluoroacetic anhydride (0.19 g, 0.89 mmol) and 90% hydrogen peroxide (28 mg, 0.74 mmol)] in dichloromethane (10 ml) was stirred at 0 °C for 20 min. Work-up in the usual manner gave an oil (72 mg) which contained (^{1}H n.m.r. analysis) starting material (50%), the *cis*-bis(trifluoroacetate) (11), the hydroxytrifluoroacetate (10), and *cis*-cyclohexane-1,2-diol (12).

Repetition of the reaction using trifluoroperacetic acid (10 mol. equiv.) gave a product which still contained starting material (50%). Repetition of the experiment using trifluoroperacetic acid (2.4 mol. equiv.) and dichloromethane–trifluoroacetic anhydride (5 mol. equiv.) gave a mixture of the *cis*-bis(trifluoroacetate) (11), the hydroxytrifluoroacetate (10), and *cis*-cyclohexane-1,2-diol (12). Control experiments resulted in recovery of starting material when (2) was treated with trifluoroacetic anhydride or with trifluoroacetic acid (75% and 80%, respectively) under identical conditions.

(b) The original experiment was repeated and the mixture was stirred at 20 °C for 3 h. The crude product [>95% of one compound (g.l.c.)] was reduced with lithium aluminium hydride. Work-up gave *cis*-cyclohexane-1,2-diol (12) (90%).

Reaction of Iodine(III) *Trifluoroacetate with Cyclohexene.*—Cyclohexene (0.36 g, 4.4 mmol) was added dropwise to iodine(III) trifluoroacetate (2.04 g, 4.4 mmol) in pentane (30 ml). A strong iodine colour developed 30 s after addition was complete and the mixture was poured into water. Work-up gave an oil (1.4 g) which contained (^{1}H

n.m.r.,[21] g.l.c.) *cis*-1,2-cyclohexylene bis(trifluoroacetate) (90%), *trans*-1,2-cyclohexylene bis(trifluoroacetate) (4%), and a mixture of minor products (4%).

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