Absolute Configuration and Chiroptical Properties of 8-Methyl-1-decalones

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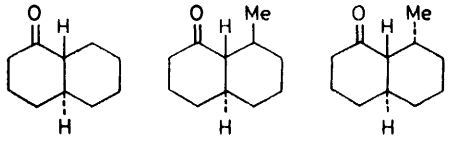
(8*S*,9*R*,10*S*)-(+)- and (8*R*,9*R*,10*S*)-(−)-8-methyl-1-decalones were prepared and their absolute configurations were determined by a kinetic resolution method. The contribution of the methyl substituent was octant consignate but different in magnitude for the axial and equatorial groups, though they were nearly mirror images with respect to the horizontal symmetry plane of the carbonyl group. The *trans*-decalone (3) was less stable than the *cis*-isomer (15). This agreed well with the result from conformational analysis.

RECENTLY, some advances in the Octant Rule have been made from both theoretical and experimental points of view.[1] One of the most notable developments was the demonstration of the necessary existence of a third surface dividing front and rear octants.[2] In connection with this, Kirk and Klyne [1a] estimated the octant-consignate contribution, $\delta\Delta\varepsilon$, of the 8-methyl substituent on the extended 8-methyl-*trans*-1-decalone to be 0.2, assuming that axial/equatorial distinction of the substituents was unimportant. Kirk [1a] and Bull [2j] have reported octant-consignate behaviour of the 6β-methyl substituent on the 5α-cholestan-4-one framework. However, the 4β-methyl substituent was shown to be octant-dissignate from the data of 4β-methyl-5α-cholestan-6-one and 5α-cholestan-6-one.[2j] In these compounds, a 1,3-diaxial interaction between the methyl groups at C-6 and C-10 or C-4 and C-10 would cause deformation of the *trans*-decalone framework. Therefore, optically active *trans*-8-methyl-1-decalones lacking a 1,3-diaxial interaction are especially well suited for an estimation of the contribution of the 8-methyl group.

House and Thompson reported that 8β-phenyl-*trans*-1-decalone was epimerized to the more stable ketone 8β-phenyl-*cis*-1-decalone by treatment with base or by being passed through either an alumina or gas chromatography column.[3] We were interested in determining the energy difference between 8β-methyl-*trans*-1-decalone and 8β-methyl-*cis*-1-decalone.

The present paper describes the synthesis, determination of the absolute configuration, and chiroptical



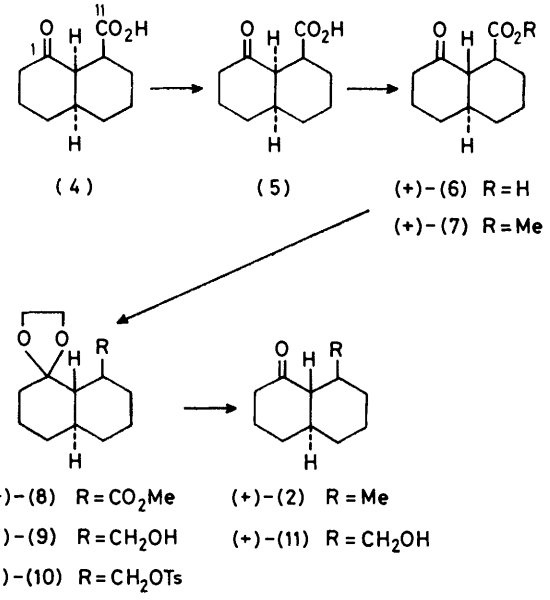
(1) (2) (3)

properties of (8*S*,9*R*,10*S*)-(+)-8-methyl-*trans*-1-decalone (2), (8*R*,9*R*,10*S*)-(−)-8-methyl-*trans*-1-decalone (3), and (9*R*,10*S*)-(+)-*trans*-1-decalone (1) † as a reference, and the relative stabilities of the *cis*- and *trans*-ring junctures of (2).

RESULTS AND DISCUSSION

Synthesis of (8S,9R,10S)-(+)-8-*Methyl*-1-*decalone and* (8R,9R,10S)-(−)-8-*Methyl*-1-*decalone*.—The diene-carboxylic acid (4) has been synthesized through several steps from the Diels–Alder adduct of pentadienoic acid and *p*-benzoquinone by Woodward and his co-workers.[4] Later, (±)-*trans*-1-decalone-8β-carboxylic acid (6) was prepared from (4) by other groups.[5]

The *trans*-keto-acid (6) was resolved with cinchonidine to give the (+)-isomer {$[\alpha]_D^{23}$ +31.8° (MeOH)}; from the mother-liquor, the (−)-isomer was obtained. But the *cis*-1-decalone-8β-carboxylic acid (5) could not be resolved even with several different optically active amines.



(4) (5) (+)-(6) R=H (+)-(7) R=Me

(+)-(8) R=CO_2Me (+)-(2) R=Me

(+)-(9) R=CH_2OH (+)-(11) R=CH_2OH

(+)-(10) R=CH_2OTs

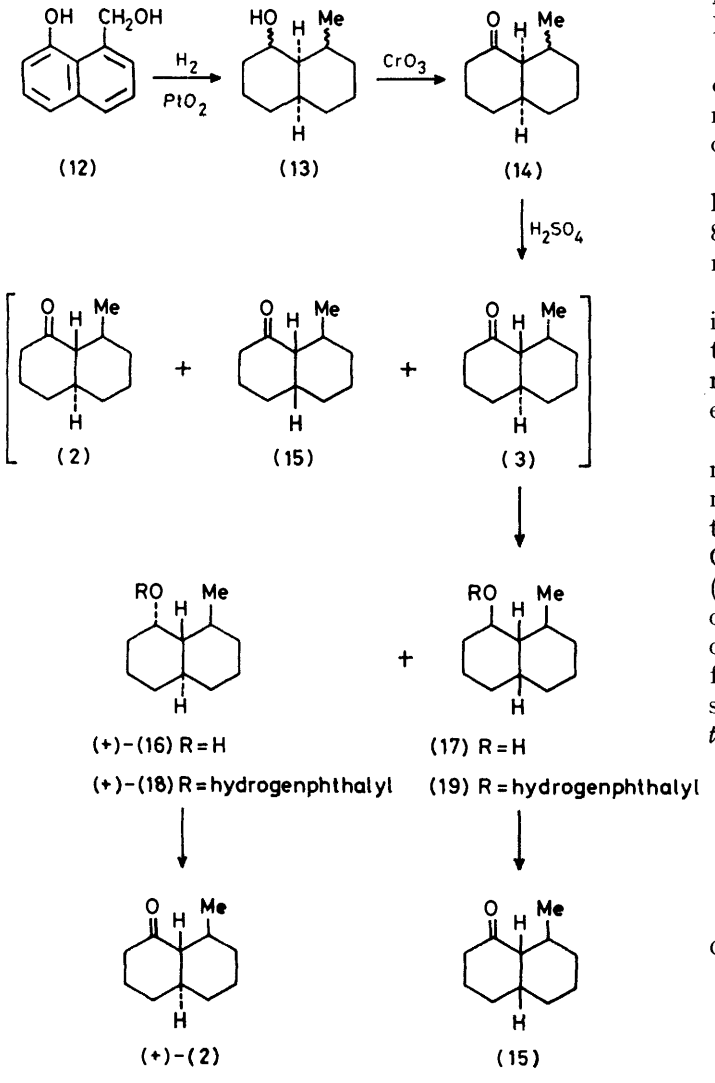
SCHEME 1

(+)-8β-Methyl-*trans*-1-decalone (+)-(2) was obtained from the keto-acid (+)-(6) by the route shown in Scheme 1.

On the other hand, 8-hydroxymethyl-1-naphthol (12) [6] was hydrogenated with Adams catalyst in acetic acid to give a mixture of 8-methyl-1-decalols, mainly composed of *cis*-ring-fused isomers. In order to increase the amounts of the *trans*-ring-fused isomers, the decalols were oxidized to the ketones and then isomerized with sulphuric acid to an equilibrium mixture. Still composed of several components, as was shown in the similar

† The systematic name for compound (1) is *trans*-octahydronaphthalen-1(2*H*)-one.

equilibrium reaction of 1-decalone (1) [7] or 8-phenyl-1-decalone,[3] the equilibrated ketones were reduced to a mixture of alcohols, mainly (16) and (17), and then isolated as 8β-methyl-*trans*-1α-decalyl hydrogenphthalate (18) and 8α-methyl-*cis*-1β-decalyl hydrogenphthalate (19) in the ratio *ca.* 6 : 1. The *trans*-hydrogenphthalate (18) was resolved with (+)-1-phenylethylamine to give the (−)-isomer, and the (+)-isomer was obtained using



SCHEME 2

(−)-1-phenylethylamine. The *cis*-hydrogenphthalate (19), however, could not be resolved even with several different amines.

(+)-8-Methyl-*trans*-1-decalone (+)-(2) was prepared by hydrolysis of the (+)-hydrogenphthalate (+)-(18) followed by oxidation with Jones reagent.

Methylmagnesium iodide was added to a mixture of the octalones (20) and (21) [3,8] in the presence of copper(I) ion. The conjugate addition products (3) and (15) were obtained and then reduced to the alcohols (22) and (17), which were esterified with camphanic acid.[9] The diastereoisomerically pure (−)-ester (23), isolated by fractional recrystallization, gave (8*R*,9*R*,10*S*)-(−)-8-methyl-1-decalone (−)-(3), $[\alpha]_D^{23}$ −91.5 (hexane) as shown in Scheme 3. The ketone (−)-(3) was equilibrated to (−)-(3) and (8*R*,9*S*,10*S*)-(+)-8-methyl-1-decalone (+)-(15) by heating with acid; (+)-(15) was then isolated by preparative t.l.c. on silica gel.

Ring-closure of 3-(pent-4-enyl)cyclohexanone to the decalones (2) and (3) was carried out according to the literature procedure,[10] but was found to be unsuitable for large-scale preparations.

trans-1-Decalol (25) was resolved with camphanyl chloride to give the (−)-isomer by a more convenient method than that reported by other groups [10,11] and converted into (+)-*trans*-1-decalone (+)-(1) by oxidation.

Determination of the Absolute Configuration.—Since the keto-acid (6) has been determined to be *trans*-1-decalone-8β-carboxylic acid,[2] the structure of the decalone (2) must be 8β-methyl-*trans*-1-decalone.

The i.r. and n.m.r. spectra of the ketone (15) were not identical with those of the ketones (2) and (3). When treated with base or acid, the ketone (3) gave an equilibrium mixture of ketones (3) and (15), which were epimeric at C-9.

Further, in the n.m.r. spectra of the alcohol (22), the reduction product of (3), the signals attributable to methylene protons were broad and similar in appearance to those of the *trans*-ring-fused decalols (16) and (25). On the other hand, alcohol (17), the reduction product of (15), gave a sharper signal due to easy mobility of the decalin ring, as observed in other *cis*-ring-fused decalin derivatives.[12] This showed that ketone (3) has a *trans*-fused-ring system and ketone (15) a *cis*-fused-ring system. The methyldecalols (16) and (23) thus have *trans*-fused-rings. In the n.m.r. spectrum of (16), the signal attributable to the proton at C-1 is sharper ($W_{\frac{1}{2}}$ 6 Hz) and at lower field (δ 4.1) than that of (22) ($W_{\frac{1}{2}}$ 19 Hz and δ 3.4).[12] The methyldecalols (16) and (22) were determined to have an axial and an equatorial hydroxy-group, respectively.

TABLE 1

Results of kinetic resolution

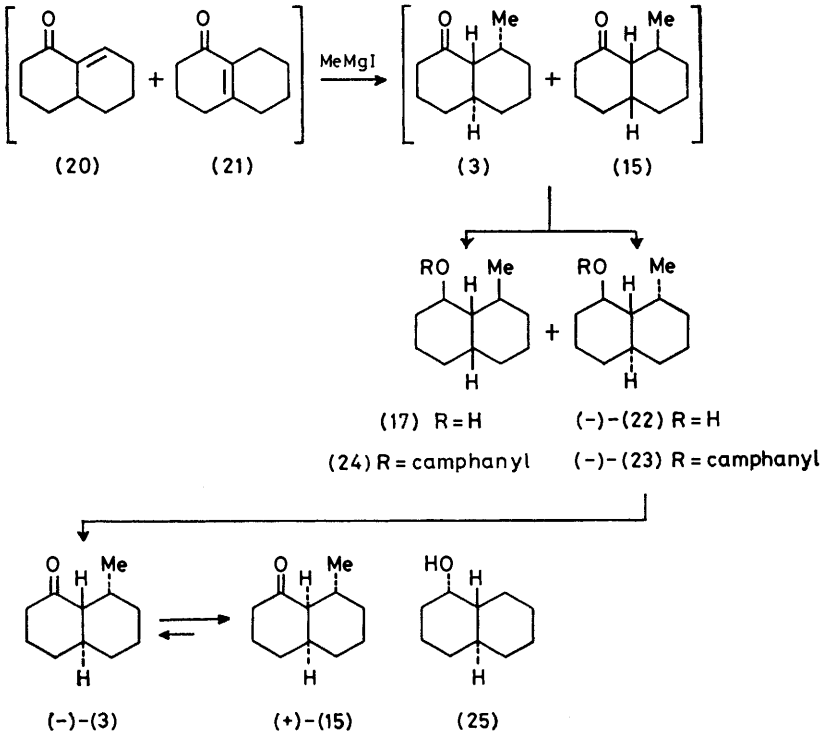
		2-Phenylbutanoic acid		
Compound	Molar ratio (anhydride : alcohol)	Enantiomeric excess * (% e.e.)	Configuration	Configuration of the alcohol
(+)-(16)	1 : 1	0.3		
(−)-(22)	1 : 1	14.4	(+)-(*S*)	1*R*,8*R*,9*R*,10*S*
(−)-(25)	1 : 1	11.7	(+)-(*S*)	1*R*,9*R*,10*S*

* These values were obtained from isolated phenylbutanoic acid, without considering the esterification yield.

The kinetic-resolution technique of Horeau [13] was applied to (−)-8β-methyl-*trans*-1α-decalol [(−)-(16)] and (−)-8α-methyl-*trans*-1β-decalol [(−)-(22)], since it is known to be useful for determining the absolute configuration of secondary alcohols. (1*R*,9*R*,10*S*)-(−)-*trans*-1-Decalol (−)-(25) was also examined to check whether the application was appropriate. The results are shown in Table 1.

The enantiomeric excess (e.e.) of recovered acid was large enough to determine the absolute configuration of the two alcohols (—)-(22) and (—)-(25) possessing an equatorial hydroxy-group. The absolute configuration of (—)-(25) was deduced to be 1*R*,9*R*,10*S* from the positive sign of the recovered acid and is the same as reported previously.[7,10,14] Thus, the (—)-alcohol (—)-(22) has the 1*R*,8*R*,9*R*,10*S* configuration and the ketone

Since the enantiomeric excess is not always satisfied, the technique of the glucoside shift in the ^{13}C n.m.r. spectrum was applied.[17] Carbon-13 signals of the (—)-decalol (16) and its α- and β-tetra-*O*-acetyl-*O*-D-glucosides were assigned using known chemical shifts [18,19] and the ^{1}H single-frequency off-resonance decoupling technique. Tetra-*O*-acetyl glucoside shifts are listed in Table 2. Consulting the glucoside shift rule for second-



SCHEME 3

(—)-(3) is 8*R*,9*R*,10*S*. The absolute configuration of (+)-(16) could not be deduced due to the very small enantiomeric excess. Consideration of a model showed that the small value may be due to the similar bulkiness of the groups around the axial hydroxy-group. To obtain the epimer of (16) at C-1, reduction was tried with various reagents and conditions, but did not give satisfactory results.

We have already shown that the absolute configuration of an optically active carboxylic acid chloride or anhydride bearing an asymmetric centre at the α-position can be deduced from the observation of the enantiomeric excess of the recovered secondary alcohol used under the same esterification conditions.[15] This method was applied to the anhydride of the (+)-keto-acid (+)-(6), a precursor of (+)-(2), using 1-phenylethyl alcohol. The recovered alcohol showed $[\alpha]_D^{22}$ +1.41 (MeOH), which corresponded to 3.4% e.e.[16] without taking the yield into consideration. Thus, the absolute configuration of (+)-(6) was deduced to be 8*S*,9*S*,10*S* and that of the (+)-ketone (+)-(2), 8*S*,9*R*,10*S*.

ary alcohols,[17] we can assign the absolute configuration of the (—)-alcohol (—)-(16) as 1*S*,8*S*,9*R*,10*S*. This leads us to 8*S*,9*R*,10*S* as the absolute configuration of the (+)-ketone (+)-(2), which coincides with that found above *via* the kinetic resolution method.

C.d. Spectra.—Table 3 lists the u.v. and c.d. values of

TABLE 2

Tetra-*O*-acetyl glucoside shifts [δ/$CDCl_3$]

	(—)-(17) Tetra-*O*-acetyl-β-D-glucoside	(—)-(17) Tetra-*O*-acetyl-α-D-glucoside
$\Delta\delta_s$[C-1′]	−2.97	−0.07
$\Delta\delta_A$[C-1]	+5.52	+7.67
$\Delta\delta_A$[C-9]	−0.41	−0.47
$\Delta\delta_A$[C-2]	−4.32	−2.35

the prepared compounds in both hexane and methanol. By assuming additivity of effects of substituents, the contributions of δΔε can be estimated as in Table 4. Apparently, contributions of the examined substituents were octant-consignate as was pointed out previously.[2]

In spite of the nearly mirror image of the axial and the equatorial methyl substituents with respect to the

horizontal symmetry plane of the carbonyl group (from consideration of models, the contribution of the equatorial methyl group was more than twice as large as that of the axial methyl group. As shown in the octant-dissignate behaviour of 4β-methyl group for 4β-methyl-5α-cholestan-6-one,[2j] this discrepancy can be ascribed largely to the deformation caused by the non-bonded interactions of axial methyl groups.

Kirk *et al.* published data on the contribution of ring D plus the methyl substituent at C-18 of a D-homo-7-oxo-steroid (δΔε 0.65).[2e] The contribution of the equatorial methyl substituent (δΔε 0.62) is similar in both sign and magnitude to that of ring D. This indicates that the interaction of a front octant substituent with the carbonyl group operates through space and falls off very rapidly with distance, as Kirk *et al.* have pointed out before.[1a,2e]

In both the 8-axial and 8-equatorial-methyl-*trans*-1-decalones, (+)-(2) and (−)-(3), the value of δΔε in methanol was about 1.5 times as large as that in hexane. This is due to dissymmetric solvation as was pointed out by Kirk *et al.*[20] On the other hand, in the compound (+)-(11), the value of δΔε for an equatorial hydroxymethyl substituent did not show a solvent effect. This behavior may result from an intramolecular hydrogen bonding between the closely located carbonyl and hydroxymethyl groups.

(8*R*,9*S*,10*S*)-(+)-8-Methyl-1-decalone (+)-(15) may have two chair forms (15a) and (15b) (Figure). But the difference of the Δε value in hexane and in methanol was

TABLE 3

U.v. and c.d. spectra of 1-decalones

Compound	Solvent	U.v., λ/nm (ε)	C.d., λ/nm (Δε)
(9*R*,10*S*)-(+)-(1)	MeOH	287 (25.1)	291 (−0.95)
	Hexane	315 (9.95)	305 (−0.462)
		305 (18.1)	295 (−0.779)
		295.5 (21.4)	286 (−0.812)
		290 (20.4)	
(8*S*,9*R*,10*S*)-(+)-(2)	MeOH	290 (27.0)	292.5 (−1.85)
			220.0 (−0.016)
			195 [a] (+1.16)
	Hexane	315sh [b] (11.3)	314sh (−0.830)
		305 (19.1)	305 (−1.39)
		297 (22.0)	297 (−1.43)
			220 (−0.016)
			192 (−2.72)
(8*R*,9*R*,10*S*)-(−)-(3)	MeOH	288 (24.0)	327 (+0.0073)
		227sh (12.7)	295 (−0.536)
			190 [a] (−2.37)
	Hexane	318sh (9.22)	332 (+0.0076)
		307 (16.8)	318.5 (−0.252)
		298 (19.9)	308 (−0.491)
		290 (19.3)	299 (−0.527)
		223 (10.0)	291 (−0.430)
			189 (−3.02)
(8*R*,9*S*,10*S*)-(+)-(15)	MeOH	290 (26.1)	296 (+1.37)
	Hexane	305sh (18.2)	320 (+0.691)
		297 (20.9)	308 (+1.18)
		291sh (20.5) *	300 (+1.26)
			293 (+1.07)
			190 (+3.55)
Equilibrium mixture of (−)-(3) and (+)-(15)	MeOH		296 (+0.603)
			245 (−0.012)
			218 (+0.045)
(8*S*,9*S*,10*S*)-(+)-(6)	MeOH	284 (28.4)	299sh (−1.09)
			289 (−1.09)
			283sh (−1.28) *
			212 (−1.58)
(8*S*,9*S*,10*S*)-(+)-(7)	MeOH	280sh (27.9)	298sh (−1.13)
			290 (−1.38)
			284 (−1.31)
			208 (−0.38)
	Hexane	311sh (8.7)	311 (−0.61)
		300 (17.2)	301 (−1.15)
		290 (21.2)	292 (−1.23)
		285 (21.8)	285sh (−1.08) *
		207 (330)	208 (−1.89)
(8*S*,9*S*,10*S*)-(+)-(11)	MeOH	288 (22.6)	293 (−1.50)
			198 [a] (+1.58)
	Hexane	291 (19.3)	302sh (−1.46)
			295 (−1.49)
			204 (+0.45)

[a] Lowest recorded value, not a maximum. [b] sh = Shoulder.

TABLE 4

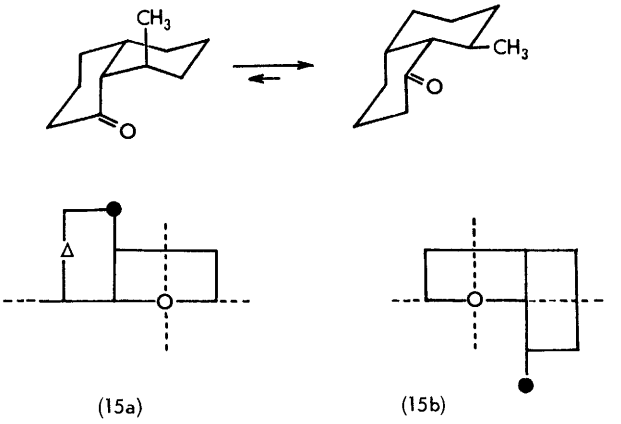
Contributions of substituents

	δΔε in MeOH	δΔε in hexane
eq-Me	0.90 *	0.62 *
ax-Me	0.41 *	0.29 *
eq-CO_2	0.42 *	
eq-CO_2Me	0.43 *	0.57 *
eq-CH_2OH	0.60 *	0.68 *
D-homo-ring	0.98 *	0.65 * (ref. 2e)

* Octant-consignate.

in the range of the solvent effect of conformationally rigid decalone derivatives.[1a] Temperature-dependent c.d. spectra (Table 3) were taken in methylcyclohexane–isopentane (1 : 5) and the data are listed in Table 5.

Conformation (15a) has a dissignate β-axial methylene



Δ = atom in front octant, negative contribution.

● = atom, negative contribution.

FIGURE Conformational isomers of (+)-(15) and their octant projections.

group and a front octant consignate methylene group. Assuming that the contribution of a C–CH_2 bond is equivalent to that of a C–CH_3 bond in the same position, one can deduce that conformation (15a) shows a small negative Cotton effect with the aid of the group contribution reported by Kirk.[1] In another conformation (15b), the main contributions are from an α-axial methylene group and a dissignate β-axial methyl substituent and are expected to show a positively signed Cotton effect in

TABLE 5

Temperature-dependent c.d. spectra [in methylcyclohexane–isopentane (1 : 5)] of (+)-(15)

Temperature (°C)	λ/nm	Δε
+25	299.5	+1.01
−68	308.5	+1.17
	298	+1.24
−190	307	+1.30
	297	+1.27

the range of 1 to 1.5 in Δε. The Δε value at −190° agreed well with that expected for conformer (15b). Further, assuming that the entropy change for (15a) ⇌ (15b) is zero, the free energy calculated using the method of Cotterill and Robinson [21] is expected to favour the conformer (15b) by 1.6 kcal mol^{-1}. This value agrees well with the free energy change of 1.6 kcal mol^{-1} deduced from the temperature-dependent c.d. spectra of (15).

Relative Stability of the cis- *and* trans-*Ring-junction of* 1-*Decalones*.—(+)-*trans*-1-Decalone (+)-(1) was equilibrated with base to give a **3.3 : 96.7** in favour of the *trans*-fused-ring system.

Equilibration of (+)-8-methyl-*trans*-1-decalone (+)-(2) with the *cis*-isomer demonstrated an essential preference for the *trans*-isomer (+)-(2), since the $[\alpha]_D$ value did not show any significant change.

On the other hand, (−)-8-methyl-*trans*-1-decalone (−)-(3) gave a mixture of (−)-(3) and (+)-8-methyl-*cis*-1-decalone (+)-(15) in a ratio of **37.1 : 62.9**. The same ratio was also observed by h.p.l.c. analysis of the equilibrium mixture obtained from 8β-methyl-*cis*-1-decalone (15) under the same reaction conditions.

We calculated the *cis* : *trans* ratio at equilibrium using

TABLE 6

cis : *trans* Ratio at equilibrium

Compound	Ratio (*cis* : *trans*) Found	Calc.
(+)-(1)	3.3 : 96.7 *	2.2 : 97.8
(+)-(2)	*ca.* 0 : *ca.* 100	1.2 : 98.8
(−)-(3)	62.9 : 37.1	74.6 : 25.4

* Prelog *et al.* reported a ratio 5 : 95.[7]

the parameters of Cotterill and Robinson,[20] and list them in Table 6 with the experimentally obtained ones. The calculated values agree well with the experimental values. The n-skew butanal interaction plays a important role in destabilizing the *trans*-isomer of (−)-(3).

EXPERIMENTAL

I.r. spectra were recorded on a JASCO-DS-402G grating spectrophotometer. Optical rotations were determined with a Perkin-Elmer model 141 polarimeter using a 1-dm microcell. Circular dichroism curves were obtained using a JASCO model J-40C spectropolarimeter. ^{1}H N.m.r. spectra were measured with a Varian A56/60 D spectrometer using tetramethylsilane as internal standard, and ^{13}C n.m.r. spectra were measured with a Varian NV-14 spectrometer. U.v. spectra were obtained on a Hitachi model 323 spectrometer.

Optical Resolution of trans-1-*Decalone*-8β-*carboxylic Acid* (6).[5]—A solution of the *trans*-keto-acid (6) (20.1 g) in methanol (70 ml) was added in one portion to a warm solution of cinchonidine (30.2 g) in methanol (100 ml). The solution was concentrated until crystals appeared. Ethyl acetate (80 ml) was added, and the mixture was then allowed to stand at room temperature for 2 h. The crystals were collected by filtration and recrystallized twice from methanol–ethyl acetate to give the pure diastereoisomeric salt (13.7 g); $[\alpha]_D^{23}$ −70.4 ± 0.9° (MeOH, *c* 1.280), m.p. 212 °C. The salt was added to a mixture of dilute hydrochloric acid and ethyl acetate. The mixture was shaken and the organic phase was separated. The aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with water, dried over anhydrous sodium sulphate, and concentrated *in vacuo*. The residue was crystallized from ether–n-hexane and gave a colourless acid, 4.93 g (49.1%), m.p. 83—84 °C; $[\alpha]_D^{23}$ +31.8 ± 0.6° (MeOH, *c* 1.338); $\nu_{max.}$ (Nujol) 1 705 cm^{-1} (Found: C, 67.2; H, 8.2. $C_{11}H_{16}O_3$ requires C, 67.3; H, 8.2%).

All the mother-liquors were collected and the crystalline salt was collected by filtration. The filtrate was concentrated to dryness then dilute hydrochloric acid was added. The mixture became clear, then crystals appeared. After 2 h, the crystals (5.5 g) were collected by filtration, washed with water, and dried, $[\alpha]_D^{25}$ 0° (McOH, *c* 0.950).

The filtrate was extracted with ethyl acetate and treated as usual. The residue was crystallized from ether (082 g); $[\alpha]_D^{23}$ −1.90 ± 0.5 (MeOH, *c* 1.113).

The filtrate was recrystallized twice from ether–n-hexane to give the antipode (2.75 g, 27.4%); $[\alpha]_D^{23}$ −30.5 ± 0.5 (MeOH, *c* 1.723) which was 95.9% optically pure.

Methyl (8S,9S,10S)-(+)-1-*Decalone*-8-*carboxylate* (+)-(7).—The (+)-keto-acid (+)-(6) (4.85 g) was treated by the procedure cited in the literature for the racemic keto-acid (6).[5] The residue was distilled at 107—110 °C at 0.7 mmHg giving a colourless oil (5.1 g, 98.1%); $[\alpha]_D^{23}$ +30.1 ± 0.6 ($CHCl_3$, *c* 1.234); $\nu_{max.}$ (neat) 1 735 and 1 713 cm^{-1}, δ ($CDCl_3$) 1.0—2.6 (m) and 3.65 (3 H, s) (Found: C, 68.3; H, 8.7. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.65%).

The Acetal of Methyl (8S,9S,10S)-(+)-1-*decalone*-8-*carboxylate* (+)-(8).—Boron trifluoride–ether (20 ml) was added dropwise to a mixture of the keto-ester (+)-(7) (5.0 g) in ethylene glycol (100 ml). The mixture was allowed to stand at room temperature for 18 h. Chloroform and then water were added. The organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phases were washed with aqueous sodium hydrogencarbonate and water, dried over anhydrous sodium sulphate, and concentrated *in vacuo* to yield an oil (6.3 g, quantitative); $[\alpha]_D^{23}$ +43.0 ± 0.6 ($CHCl_3$, *c* 1.362), which was used for the next reaction without further purification; $\nu_{max.}$ (neat) 1 730 cm^{-1}.

The Acetal of (8S,9S,10S)-(+)-8-*Hydroxymethyl*-1-*decalone* (+)-(9).—A solution of the (+)-ester (+)-(8) (6.3 g) in dry tetrahydrofuran (30 ml) was added to a slurry of lithium aluminium hydride (1.7 g) in tetrahydrofuran (20 ml) with cooling in ice in a nitrogen atmosphere. The mixture was warmed gradually and heated under reflux for 6 h, then any excess of lithium aluminium hydride was decomposed with methanol–ether and then with 20% aqueous sodium hydroxide. The mixture was extracted with ether. The solution was washed with water, dried over anhydrous sodium sulphate, and concentrated *in vacuo*, giving a viscous oil (4.7 g, 83.8%); $\nu_{max.}$ (neat) 3 400 cm^{-1}; δ ($CDCl_3$) 0.7—1.9 (m), 2.72 (1 H, dd, *J* 5.10 Hz), 3.28 (1 H, t, *J* 5.0 Hz), and 4.00 (2 H, s). The product was used for the next reaction without further purification.

(8S,9S,10S)-(+)-8-*Methyl*-1-*decalone* (+)-(2).—A solution of freshly recrystallized toluene-*p*-sulphonyl chloride (0.48 g) in dry pyridine (7 ml) was added dropwise to a solution of the (+)-alcohol (+)-(9) (0.50 g) in pyridine (3 ml) at −5 to −7 °C during 40 min. The mixture was then stirred at 0 °C for 2 h, and ice-cold water was added. The crystals of (+)-(10) (0.5 g, 59.4%) were collected by filtration, washed with water, and dried, m.p. 70—72 °C (95—96 °C for the racemic compound); $[\alpha]_D^{22}$ +37.3 ± 1.2 ($CHCl_3$, *c* 0.837).

A solution of the toluene-*p*-sulphonate (+)-(10) (377 mg) in dry tetrahydrofuran (8 ml) was added to a slurry of lithium aluminium hydride (0.25 g) in tetrahydrofuran (5 ml) at 3—5 °C in a nitrogen atmosphere during 30 min. The mixture was heated under reflux for 2.5 h. Excess of lithium aluminium hydride was decomposed with methanol–tetrahydrofuran and then with 40% aqueous sodium hydroxide. The mixture was extracted with ether and concentrated by distillation. The crude acetal was shaken with dilute hydrochloric acid in acetone for 10 min. Water was added and the mixture was then extracted with ether. The solution was washed with water, dried over anhydrous sodium sulphate, and concentrated *in vacuo*. The residue (92 mg) was chromatographed on alumina (5 g, Merck Co., grade 2) in hexane and distilled at 80 °C (bath temperature) at 0.8 mmHg through a short-path distillation apparatus; $[\alpha]_D^{22}$ +84.7 ± 1.2 (MeOH, *c* 1.069), +75.0 ± 1.5 (n-hexane, *c* 0.776); $\nu_{max.}$ (neat) 1 715 cm^{-1} (Found: C, 79.25; H, 10.85. $C_{11}H_{18}O$ requires C, 79.45; H, 10.9%).

(8S,9S,10S)-(+)-8-*Hydroxymethyl*-1-*decalone* (+)-(11).—Dilute hydrochloric acid (2 ml) was added to a solution of the optically active acetal (+)-(9) (0.20 g) in acetone (3 ml). The solution was shaken for 10 min, water was added, and the mixture was then extracted with ether. The solution was treated as usual and the product, distilled at 130 °C (bath temperature) at 0.8 mmHg through a short-path distillation apparatus, gave a viscous oil (151 mg, 93.7%); $\nu_{max.}$ (neat) 3 410 and 1 724 cm^{-1}; δ ($CDCl_3$) 0.7—2.5 (m) and 3.5 (2 H, d, *J* 4.0 Hz) (Found: C, 71.25; H, 10.95. $C_{11}H_{18}O_2$ requires C, 72.5; H, 9.95%).

Reduction of 8-*Hydroxymethyl*-1-*naphthol* (12).—A mixture of 8-hydroxymethyl-1-naphthol (12) (40 g), platinum dioxide (2 g), and glacial acetic acid (300 ml) was shaken under an initial hydrogen pressure of 5 kg cm^{-2} overnight. The catalyst was removed by filtration and the filtrate was concentrated *in vacuo*. Ether was added, the solution was washed with aqueous sodium hydrogencarbonate, aqueous sodium hydroxide, and then water, dried over anhydrous sodium sulphate and concentrated *in vacuo*. The residue was distilled at *ca.* 120 °C at 0.6 mmHg, yield 21 g.

The aqueous sodium hydroxide extracts were washed with ether, acidified with concentrated hydrochloric acid, extracted with ether, and the solution was treated as usual. The product was distilled at *ca.* 150 °C at 0.4 mmHg to give a pale yellow oil (9.3 g).

Both products were again hydrogenated and purified by distillation at 75—90 °C at 1.2 mmHg to give a colourless liquid (20.0 g, 51.7%); $\nu_{max.}$ (neat) 3 440 cm^{-1}. The n.m.r. spectrum showed a mixture of two alcohols but did not show aromatic protons (Found: C, 77.95; H, 11.45. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%).

Oxidation of the Hydrogenated Products (13).—Jones reagent was added to a solution of the alcohol (13) (20 g) in acetone (100 ml) with cooling in ice until the characteristic orange colour persisted. Water (200 ml) was added, the mixture was extracted with ether, and the solution was then treated as usual. The oily residue was distilled at 65—80 °C at 1.0 mmHg to give (14) as a pale yellow liquid (17.4 g, 88.1%); $\nu_{max.}$ (neat) 1 705 cm^{-1}.

Equilibration of the Ketones (14).—A solution of the ketones (14) (17.4 g), concentrated sulphuric acid (4 ml), and methanol (150 ml) was heated under reflux for 2 h, poured into ice-cold water, then extracted with ether. The solution was washed with aqueous sodium hydrogencarbonate and water, dried over anhydrous sodium sulphate, and then concentrated by distillation. The residue was distilled at 72—78 °C at 1.8 mmHg (13.2 g, 75.9%). The n.m.r. spectrum showed that it was a mixture of ketones, probably (2), (3), and (15).

Reduction of a Mixture of Ketones (2), (3), *and* (15).—Sodium borohydride (3.0 g) was added portionwise to a solution of the above ketones (13.2 g) in methanol (100 ml) with cooling in ice. The mixture was stirred for 1 h and excess of sodium borohydride was decomposed with concentrated hydrochloric acid. Water (300 ml) was added, the mixture was extracted with ether, and the solution was treated as usual. The residue was distilled at 71—76 °C at 0.5 mmHg to give a colourless liquid [comprising (16), (18), and other hydroxy-compounds] (12.7 g, 95.1%); $\nu_{max.}$ (neat) 3 420 cm^{-1}.

8β-*Methyl*-trans-1α-*decalyl Hydrogenphthalate* (18) *and* 8α-*Methyl*-cis-1β-*decalyl Hydrogenphthalate* (19).—A mix-

ture of the above alcohols (12.7 g), freshly sublimed phthalic anhydride (11.7 g), and pyridine (100 ml) was heated under reflux for 4 h, then poured onto ice-cold hydrochloric acid and extracted with ether. The solution was washed with water, dried over anhydrous sodium sulphate, and concentrated *in vacuo*. Benzene was added and the mixture was warmed briefly. The insoluble solid (1.5 g) was removed by filtration. The filtrate was concentrated and crystallized from n-hexane (9.7 g, 40.9%); m.p. 155—160 °C. Recrystallization from benzene–petroleum raised the m.p. to 172—173 °C. This was the *trans*-isomer (18), $\nu_{max.}$ ($CHCl_3$) 1 708 and 1 292 cm^{-1}; δ ($CDCl_3$) 0.91 (3 H, d, *J* 5.5 Hz), 1.0—2.0 (m), and 4.10 (1 H, m) (Found: C, 72.15; H, 7.7. $C_{19}H_{24}O_4$ requires C, 72.15; H, 7.65%).

From the combined mother-liquors, crystals were collected and dissolved in chloroform, insoluble solids being removed by filtration. The mother-liquor was concentrated and crystallized from benzene–petroleum to give a colourless powder (1.65 g, 6.9%); $\nu_{max.}$ ($CDCl_3$) 1 706 and 1 298 cm^{-1}; δ ($CDCl_3$) 1.05 (3 H, d, *J* 6.0 Hz), 1.0—2.0 (m), 5.12 (1 H, br s), and 7.5—8.0 (m). This was the *cis*-isomer (19) (Found: C, 71.25; H, 7.6. $C_{19}H_{24}O_4$ requires C, 71.15; H, 7.65%).

Optical Resolution of 8β-*Methyl*-trans-1α-*decalyl Hydrogenphthalate* (18).—A solution of (−)-1-phenylethylamine (4.0 g) in ethyl acetate (10 ml) was added to a solution of the half-ester (18) (10.3 g) in ethyl acetate (90 ml) in one portion. The solution was allowed to stand at room temperature overnight. The crystalline salt was collected by filtration and recrystallized three times from methanol–ethyl acetate (0.90 g); m.p. 166—170 °C, $[\alpha]_D^{26}$ +91.8 ± 1.5 (MeOH, *c* 0.670).

Dilute hydrochloric acid was added to a suspension of the salt in ether. The mixture was shaken until the salt dissolved. The organic phase was separated and the aqueous phase was extracted with ether. The combined organic phases were treated as usual. The product was crystallized from n-hexane as a colourless powder (0.63 g, 31.5%); m.p. 176 °C; $[\alpha]_D^{26}$ +91.8 ± 1.4° (MeOH, *c* 0.963); $\nu_{max.}$ (Nujol) 1 728 and 1 692 cm^{-1}.

The antipodal isomer (1.5 g, 75.0%); $[\alpha]_D^{26}$ −92.3 ± 1.3 (MeOH, *c* 1.083), was obtained from the recovered monoester with (+)-1-phenylethylamine.

(1S,8S,9R,10S)-(+)-8-*Methyl*-1-*decalol* (+)-(16).—A solution of the (+)-half-ester (+)-(18) (1.5 g) in aqueous potassium hydroxide (2.0 g per 10 ml) and ethanol (10 ml) was heated under reflux for 45 h. Water was added, and the mixture was extracted with ether and treated as usual. The residue was distilled at 90 °C (bath temperature) at 0.5 mmHg through a short-path distillation apparatus (0.69 g, 87.7%); $[\alpha]_D^{26}$ +43.4 ± 0.7° (MeOH, *c* 1.229); $\nu_{max.}$ ($CHCl_3$) 3 625 cm^{-1}; δ ($CDCl_3$) 0.91 (3 H, d, *J* 5.5 Hz), 0.7—2.0 (m), and 4.1 (1 H, m); δ_C ($CDCl_3$) 19.08 (C-11), 19.93 (C-3), 26.00 (C-6), 32.52, 33.96 (C-2), 34.14 (C-8), 34.76, 35.20, 36.24 (C-10), 53.10 (C-9), and 66.03 (C-1) (Found: C, 77.85; H, 12.15. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%).

(8S,9R,10S)-(+)-8-*Methyl*-1-*decalone* (+)-(2).—The (+)-decalol (+)-(16) (134 mg) was oxidized by the procedure used for the hydrogenated product (13). The product was distilled at 70 °C (bath temperature) at 0.3 mmHg through a short-path distillation apparatus; $[\alpha]_D^{26}$ +70.6 ± 1.0 (n-hexane, *c* 1.274), +81.0 ± 1.2 (MeOH, *c* 1.021). The i.r. and n.m.r. spectra were identical to those of the ketone prepared above.

8β-*Methyl*-cis-1α-*decalol* (17).—The *cis*-half-ester (19) was treated by the procedure for the *trans*-isomer (18), m.p. 53—56 °C; $\nu_{max.}$ ($CHCl_3$) 3 620 and 1 056 cm^{-1}; δ ($CDCl_3$) 1.05 (3 H, d, *J* 6.0 Hz), 1.1—2.0 (m), and 3.75 (1 H, br s); δ_C ($CDCl_3$) 21.16, 22.31, 24.16, 25.92, 28.06, 30.02, 31.94, 36.72, 37.04, 49.54 (C-9), and 76.89 (C-1).

8β-*Methyl*-cis-1-*decalone* (15).—The *cis*-decalol (17) (200 mg) was oxidized to (15) by the procedure for the *trans*-isomer (16), yield 180 mg (91.1%); $\nu_{max.}$ (neat) 1 708 cm^{-1}; δ ($CDCl_3$) 0.8 (3 H, d, *J* 6.5 Hz) and 1.0—2.5 (m).

Reaction of a Mixture of Octal-1-ones (20) *and* (21) *with Methylmagnesium Iodide.*—Copper(I) chloride (2.3 g) was added to a solution of methylmagnesium iodide in ether [from magnesium (7.2 g), methyl iodide (42 g) and ether (300 ml)]. A solution of a mixture of octal-1-ones [3,8] (20) and (21) (22.9 g) in ether (300 ml) was added dropwise to the mixture with cooling in ice. After the mixture had been stirred for 4 h, a solution of saturated ammonium chloride and ammonia was added with cooling in ice, and the solid was filtered off and washed with ether. The organic phase was separated and the aqueous phase was extracted with ether. The combined organic phases were washed with water, dried over anhydrous sodium sulphate, and concentrated *in vacuo*. The residue (25.5 g) was chromatographed on silica gel (200 g, grade 2, Merck Co.). After collection of the non-polar compound [4.1 g, eluted with n-hexane (1.6 l)], ketones of conjugate addition (3) and (15) [eluted with benzene–hexane (1 : 1) (1.6 l)] were collected and distilled at 121—123 °C and 17 mmHg to give a colourless liquid (8.7 g), which was shown to be a mixture of methylated ketones [mainly (3) and (15)] by the i.r. and n.m.r. spectra.

From the fraction eluted with benzene, hydroxy-compounds (5.4 g) were obtained and dehydrated by distillation to the dienes (*cf.* ref. 3).

Reduction of Ketones (3) *and* (15).—Sodium borohydride (0.45 g) was added to a solution of the above mixture of 8-methyl-1-decalones (1.7 g) in methanol (20 ml) with cooling in ice. The mixture was stirred for 2 h, dilute hydrochloric acid was added, and the mixture was extracted with ether and the solution treated as usual. The residue was distilled at 73 °C and 1.5 mmHg, giving a colourless viscous oil, (17) and (22) (1.54 g, 89.5%).

Optical Resolution of 8α-*Methyl*-trans-1β-*decalol* (22).—A solution of camphanyl chloride [9] (1.0 g) in pyridine (6 ml) was added to a solution of the alcohols (17) and (22) (0.77 g) in pyridine (3 ml). The mixture was allowed to stand overnight, poured into ice-cold dilute hydrochloric acid, and extracted with ether. The solution was washed with water, aqueous sodium hydrogencarbonate, and water, then dried over anhydrous sodium sulphate and concentrated. The residue was crystallized from hexane, and then recrystallized from hexane four times to give the pure diastereoisomer, (−)-(23), yield 88.7 mg (11.1%), m.p. 165—166°; $[\alpha]_D^{22}$ −43.0 ± 1.0° ($CHCl_3$, *c* 0.882); $\nu_{max.}$ (Nujol) 1 788 and 1 741 cm^{-1}; δ ($CDCl_3$) 0.82 (3 H, d, *J* 7.0 Hz), 0.95 (3 H, s), 1.07 (3 H, s), 1.10 (3 H, s), 1.2—2.5 (m), and 4.70 (1 H, br s) (Found: C, 72.55; H, 9.3. $C_{21}H_{32}O_4$ requires C, 72.4; H, 9.25%).

A mixture of the (−)-ester (−)-(23) (86 mg), 10% aqueous potassium hydroxide (2 ml), and methanol (5 ml) was heated under reflux for 2 h, poured into water, and extracted with ether. The solution was washed with water, dried over anhydrous sodium sulphate, and concentrated *in vacuo*. The crystalline residue sublimed at 100 °C and 0.8

mmHg, giving colourless needles of (−)-(22), yield 23 mg (55.4%), m.p. 90—91 °C; $[\alpha]_D^{22}$ −50.0 ± 1.3 (MeOH, *c* 0.722); $\nu_{max.}$ (Nujol) 3 240 and 1 058 cm^{-1}; δ ($CDCl_3$) 0.92 (3 H, d, *J* 8.0 Hz), 0.8—2.4 (m), and 3.40 (1 H, br s) (Found: C, 78.4; H, 11.95. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%).

All the mother-liquor of the recrystallization was collected, concentrated *in vacuo*, and recrystallized twice from methanol. The specific rotation, $[\alpha]_D^{22}$ +6.7 ± 0.4 ($CHCl_3$, *c* 1.172), did not change with further recrystallization. The ester (268 mg) was hydrolysed as above but the alcohol was found to be a mixture of the two isomers (23) and (24) (130 mg) by t.l.c. [see next preparation, (*b*)].

(8R,9R,10S)-(−)-8-*Methyl*-1-*decalone* (−)-(3).—(*a*) The (−)-alcohol (−)-(22) (42 mg) was oxidized in the manner described for the hydrogenated product (13). The residue was distilled at 80 °C (bath temperature) and 1 mmHg through a short-path distillation apparatus. The distillate (37.6 mg, 90.1%), solidified quickly, m.p. 66—68° C; $[\alpha]_D^{23}$ −91.5 ± 0.9 (hexane, *c* 1.194), −92.4 ± 2.3 (MeOH, *c* 0.318 3); $\nu_{max.}$ (Nujol) 1 696 cm^{-1}; δ ($CDCl_3$) 0.95 (3 H, d, *J* 7.0 Hz) and 1.2—2.6 (m) (Found: C, 79.5; H, 10.85. $C_{11}H_{18}O$ requires C, 79.45; H, 10.9%).

(*b*) The mixture of two alcohols, obtained from the mother-liquor of the resolution, was oxidized as above. The ketone, $[\alpha]_D^{22}$ +33.5 ± 0.2 (MeOH, *c* 4.228), was chromatographed on a thin layer of silica gel (Merck Co., pre-coated plate F-254) in benzene. The fraction of larger R_F value (39 mg) was distilled at 100 °C (bath temperature) and 0.8 mmHg through a short-path distillation apparatus to give partially resolved *trans*-fused ketone (3); $[\alpha]_D^{21}$ +33.2 ± 0.8 (MeOH, *c* 0.979). The i.r. and n.m.r. spectra were identical with those of (−)-(3).

The fraction of smaller R_F value (38 mg) was distilled in the same manner to give partially resolved *cis*-ring-fused decalone (15); $[\alpha]_D^{22}$ +33.0 ± 0.9 (MeOH, *c* 0.886). The i.r. and n.m.r. spectra were identical with those of (15).

Equilibration of (9R,10S)-(+)-1-*decalone* (+)-(1) *with Base*.—(*a*) (+)-*trans*-1-Decalone (10.17 mg) was dissolved in 5% sodium methoxide in methanol (1.0 ml). The solution was allowed to stand at room temperature for 2 d; $[\alpha]_D^{22}$ +12.0 ± 0.6 (MeONa–MeOH, *c* 1.017).

(*b*) (+)-*trans*-1-Decalone (76.6 mg) and a solution of 5% potassium hydroxide in methanol (5 ml) were heated under reflux for 2 h, poured into water, extracted with ether, and the solution treated as usual. The oily residue was distilled at 80 °C (bath temperature) and 0.8 mmHg; $[\alpha]_D^{22}$ +12.5 ± 0.5 (MeOH, *c* 1.070).

Equilibration of Methyl Ketones (3) *and* (15).—(*a*) A solution of the methyl ketone (15) (180 mg), methanol (2 ml), and a drop of concentrated sulphuric acid was heated under reflux for 2 h. Water was added, the mixture was extracted with ether, and the solution was treated as usual. The residue was distilled at 120 °C (bath temperature) and 0.4 mmHg through a short-path distillation apparatus. The isomer ratio (3) : (15) was 1 : 2.2, according to h.p.l.c. analysis on μ-Porasil (Waters Co., 4.0 mm × 30 cm) in hexane.

(*b*) A solution of the methyl ketone (15) (42 mg) and 5% potassium hydroxide in methanol (6 ml) was heated under reflux for 1.5 h, poured into water, and extracted with ether. The solution was treated as usual and the distillate was analysed by h.p.l.c. The ratio of the two ketones was identical to that observed above.

(*c*) A solution of the (−)-methyl ketone (−)-(3) (19 mg) was treated in the same manner as in (*a*). The residue, distilled at 80 °C (bath temperature) and 0.8 mmHg, gave a colourless oil (15.1 mg), $[\alpha]_D^{22}$ +32.1 ± 0.5 (MeOH, *c* 1.510), which was chromatographed on a thin layer of silica gel (Merck Co. pre-coated plate F-254) in benzene. The fraction of larger R_F value, distilled at 80 °C (bath temperature) and 1 mmHg, gave the *trans*-isomer (3) (2.72 mg), $[\alpha]_D^{22}$ −85.3 ± 4.7 (MeOH, *c* 0.272), which was contaminated with *ca.* 5% of the *cis*-isomer (15) according to h.p.l.c. analysis.

The fraction of smaller R_F value was also distilled under the same conditions and gave the *cis*-isomer (15) (4.72 mg), $[\alpha]_D^{22}$ +105.5 ± 3.1 (MeOH, *c* 0.472). The i.r. spectrum was identical to that of the oxidized product of (17).

Treatment of (+)-(2) *with Base*.—The ketone (+)-(2), $[\alpha]_D^{27}$ +81.0 ± 1.2 (MeOH), was treated as in (*b*) above, $[\alpha]_D^{22}$ +80.8 ± 0.9 (MeOH, *c* 1.344). I.r. and n.m.r. spectra were identical to those of the starting material.

Kinetic Resolution of 2-*Phenylbutanoic Anhydride with the Alcohols* (+)-(16), (−)-(22), *and* (−)-(25).—A solution of 2-phenylbutanoic anhydride (83.6 mg) in dry pyridine (1 ml) was added dropwise to a solution of the (−)-alcohol (−)-(23) (41.6 mg) in pyridine (0.5 ml) with cooling in ice. The mixture was allowed to stand at room temperature overnight, then water (5 ml) was added, and the mixture was allowed to stand at room temperature for 2 h. Benzene (5 ml) and powdered phenolphthalein were added. The mixture was titrated against 0.1N sodium hydroxide (4 ml). The pink aqueous solution was separated, washed with benzene, acidified with concentrated hydrochloric acid, and extracted with benzene. The solution was treated as usual. The concentrated residue was dissolved in benzene (1.0 ml), α_D^{22} +0.711 ± 0.004 which was $[\alpha]_D^{22}$ +10.8 (benzene, *c* 6.562) and 32.4% e.e. when the 56.2% yield was taken into consideration. The residue was distilled at 110 °C (bath temperature) and 0.5 mmHg through a short-path distillation apparatus, $[\alpha]_D^{22}$ +13.9 ± 0.2 (benzene, *c* 3.728), which corresponded to 14.4% e.e. (Found: C, 73.3; H, 7.6. $C_{10}H_{12}O_2$ requires C, 73.15; H, 7.35%).

The other alcohols (+)-(16) and (−)-(25) were treated in the same manner. The results are shown in Table 1.

Kinetic Resolution of 1-*Phenylethanol with the Anhydride* (−)-(6).—The 93.7% optically pure (−)-keto-acid (−)-(6) (214 mg), $[\alpha]_D^{22}$ −29.8 (MeOH), was added to oxalyl chloride (1.5 g) in small portions. After the bubbling had ceased, the solution was allowed to stand for 20 min and concentrated *in vacuo*. Pyridine (3 ml) and then the (−)-keto-acid (213 mg) were added. The mixture was stirred at room temperature for 30 min and cooled in ice. A solution of 1-phenylethanol (265 mg, 2 equiv.) in pyridine (1 ml) was added. The mixture was allowed to stand overnight, poured into ice-cold water, and extracted with ether. The solution was washed with dilute hydrochloric acid and water, dried over anhydrous sodium sulphate, and concentrated *in vacuo*. The residue was distilled at 110 °C (bath temperature) and 0.3 mmHg through a short-path distillation apparatus, chromatographed on a thin layer of silica gel (Merck Co., pre-coated F-254) in benzene–ethyl acetate (2 : 1) and redistilled, $[\alpha]_D^{22}$ −1.32 ± 0.6 (MeOH, *c* 6.947), which was 3.1% e.e. and 3.4% e.e. to its optical purity.

Tetra-O-*acetyl*-α- *and* -β-D-*glucosides of* (−)-(16).—These were prepared according to the procedure of Seo and his co-workers.[17] (−)-(16) Tetra-*O*-acetyl-α-D-glucoside was a syrup, contaminated with a small amount of the β-isomer. Tetra-*O*-Acetyl-β-D-glucoside (−)-(16) had m.p. 155—156 °C; $[\alpha]_D^{25}$ −54.2 ± 0.7 (MeOH, *c* 1.458); $\nu_{max.}$ (Nujol) 1 745 and 1 045 cm^{-1}; δ ($CDCl_3$) 0.84 (3 H, d, *J* 6.0 Hz), 0.5–2.0 (m),

1.95 (3 H, s,), 2.02 (6 H, s), 2.04 (3 H, s), and 3.5—4.4 (m) (Found: C, 60.1; H, 7.7. $C_{25}H_{38}O_{10}$ requires C, 60.25; H, 7.7%).

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