[Chem. Pharm. Bull. 20(2) 314—324 (1972)] UDC 547.659.03.04

Syntheses and Spectral Properties of 2,6-Disubstituted-*trans*-decalins

KEN'ICHI TAKEDA and SADAO YAMAMOTO

Shionogi Research Laboratory, Shionogi and Co., Ltd.[1]

(Received August 18, 1971)

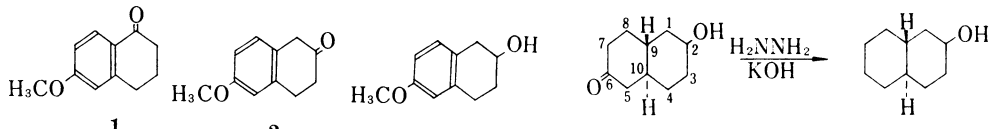
Various stereoisomers of 6-substituted-*trans*-2-decalols have been synthesized; four possible epimers for 6-methoxy and 6-chloro derivatives, three epimers for 6-cyano derivatives, and two epimers for 6-phenyl, 6-carbomethoxy, and 6-oxo derivatives were reported. The structures of these compounds were assigned by proton magnetic resonance and infrared spectroscopies. A paramagnetic shift reagent, tris(dipivalomethanato)europium (III), was successfully applied in the proton magnetic resonance spectra of the two epimers of *trans*-2-decalol to establish their structures. The spectral data obtained were also presented and discussed.

In a preceeding paper, we have shown that a dominant factor governing the acetolysis of 3-substituted A/B *trans*-11α-tosyloxysapogenins is due to inductive effect of the 3-substituents through carbon-carbon chains.[2] To confirm this remote structural influence, we decided to investigate the acetolyses of 2,6-disubstituted-*trans*-decalin system, which is rigid in the conformation and simpler in the structure than the sapogenin system. For this purpose some 6α(axial)- and 6β(equatorial)-substituted-2-hydroxy-*trans*-decalin derivatives[3] were synthesized and their configurations were assigned by infrared (IR) and proton magnetic resonance (PMR) spectroscopies. The present paper describes this.

Result and Discussion

Synthesis of 6-Substituted-2-hydroxy-*trans*-decalin Derivatives

The starting material, 6-methoxy-2-tetralone (**2**), was obtained from 6-methoxy-1-tetralone (**1**) by the method of Nagata and Terasawa[4] and lithium aluminum hydride reduction of **2** afforded 2-hydroxy-6-methoxy-tetralin (**3**). Compound **3** was converted to 2α- and 2β-hydroxy-*trans*-6-decalones (**4e** and **4a**) by the procedure of Clarke and Martin.[5] The Wolff-Kishner reduction of **4e** and **4a** gave 2α- and 2β-*trans*-decalins (**5e** and **5a**) (Chart 1).



1 2 3 4a (a = 2-axial) 4e (e = 2-equatorial) 5a 5e

Chart 1[3]

An identification and purity check of all the derivatives prepared were achieved by gas liquid chromatography (GLC) using polar and non-polar stationary phases. These GLC studies will be reported elsewhere.

1) Location: *Fukushima ku, Osaka.*
2) K. Takeda, H. Tanida and K. Horiki, *J. Org. Chem.*, **31**, 734 (1966).
3) Nomenclature in this paper uses the decalin conventions and numbering, with the hydrogen at C_9-atom in the β-orientation. To simplify the nomenclature of the compounds used, the following symbols are used; for 6α- and 6β-substituted-*trans*-decalin-2α-hydroxy derivatives, 6-ax·R-2-eq·OH and 6-eq·R-2-eq·OH. All the compounds in the present study are *dl* mixtures.
4) W. Nagata and T. Terasawa, *Chem. Pharm. Bull.* (Tokyo), **9**, 267 (1961).
5) R.L. Clarke and C.M. Martin, *J. Am. Chem. Soc.*, **81**, 5716 (1959).

The configuration of the substituents at C_2- and C_6-atoms of all the derivatives synthesized in this study were determined on the basis of IR and/or PMR spectral methods. This will be discussed later in this paper.

a) 6α- and 6β-Methoxy Derivatives (Chart 2)——The direct O-methylation of **6e** and **6a** with methylsulfinyl carbanion and methyl iodide in dimethyl sulfoxide afforded **8e** and **8a** in good yield (95—98%). Compounds **8e** and **8a** were reduced with lithium tri-tertiary butoxyaluminum hydride, a stereospecific reducing reagent.

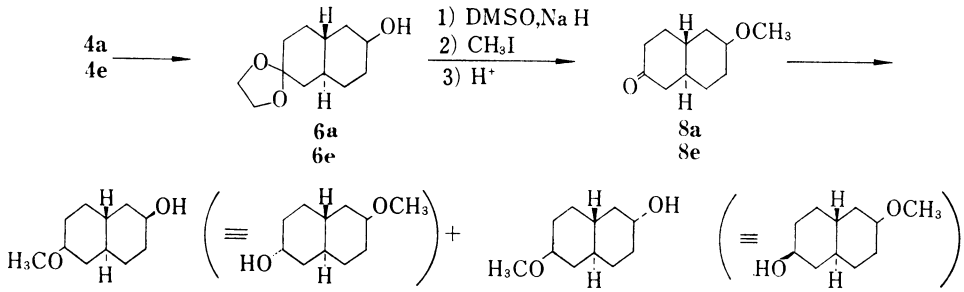


Chart 2

b) 6α- and 6β-Phenyl Derivatives (Chart 3)——Grignard reaction **4e** with phenylmagnesium bromide gave a mixture of 6-eq·Ph-6-ax·OH- and 6-ax·Ph-6-eq·OH-2-eq·OH. In accordance with earlier reports,[6,7] treatment of the epimeric products **10** with W-2 Raney nickel in ethanol at room temperature led to **11ea** and **11ee**. GLC analysis showed that the mixture was approximately 63/37 (**11ee**/**11ea**) ratio.

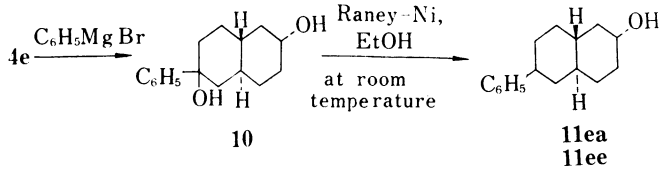


Chart 3

c) 6α- and 6β-Chloro Derivatives (Chart 4)——The chlorination of equatorial and axial alcohols was achieved with phosphorous pentachloride in the presence of calcium carbonate, but was unsuccessful with thionyl chloride under similar reaction conditions. Reaction of **6e** with PCl_5 at 0——5° gave **12a** (yield 87%, by GLC) and an olefinic compound (12%, by GLC). Reaction of **6e** under the same conditions gave only an olefinic compound. At lower temperature (—10——15°), **12e** was obtained in low yield. The product ratio was **12e** (33%), olefin (49%) and unreacted starting material (18%). Tri-tertiary butoxyaluminum hydride reduction of these 6-ketones (**12a** and **12e**) followed by column chromatography and preparative thin-layer chromatography (TLC) gave pure samples of four epimeric compounds (**13aa**, **13ae**, **13ea**, and **13ee**).

These results suggest that substitution reaction of the 2-equatorial hydroxy compound proceeds by a bimolecular reaction mechanism (SN_2) with inversion of configuration at the

6) J.A. Zderic, Ma. E.C. Rivera and D.C. Limon, *J. Am. Chem. Soc.*, **82**, 6373 (1960).
7) E.W. Garbisch, Jr., *J. Org. Chem.*, **27**, 3363 (1962).

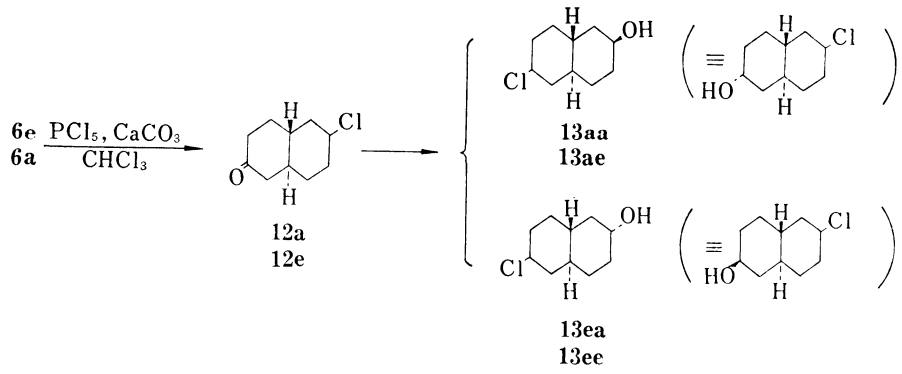


Chart 4

C_2-atom. On the other hand, in the chlorination of the 2-axial hydroxy compound anti-coplaner elimination reaction predominates to give the olefins.

d) 6α- and 6β-Carbonitrile, and Methyl 6β-Carboxylate Derivatives (Chart 5)——Recently, using N-methylpyrrolidone containing *t*-butyl alcohol (5%), nitriles were obtained in good yield from the reaction of some steroidal secondary *p*-toluene sulfonates with sodium cyanide.[8] We prepared the 2-axial-carbonitrile (**15a**) in a 48% yield from 2-equatorial-*p*-toluene sulfonate (**14e**) by the method mentioned above, but the reaction of 2-axial-*p*-toluene sulfonate afforded rather olefinic by-product.

In analogy with the chlorination of the 2-axial hydroxy compound, anti-coplaner elimination reaction will take place predominantly.

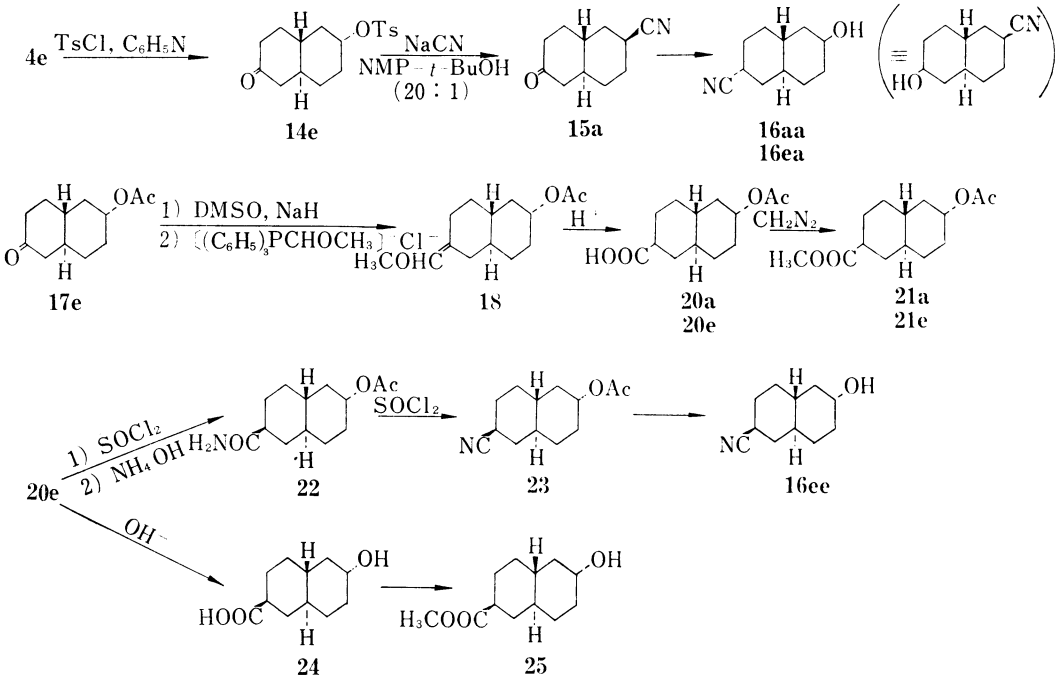


Chart 5

8) H.B. Henbest and W.R. Jackson, *J. Chem. Soc.*, **1962**, 954.

The reduction of *trans*-2β-cyano-6-decalone (**15a**) with lithium tri-tertiary butoxyaluminum hydride and with sodium borohydride afforded mixtures of epimeric alchols (**16aa** and **16ea**) in the product ratios 92/8 and 81/19, respectively.

Accordingly, we synthesized the required 6β-carbonitrile derivative *via* the 6β-carboxamide compound. The *trans*-2α-acetoxydecalin-6-carboxylic acids (**20**) were prepared from **17e** by the Corey's variation[9] of the Wittig reaction followed by the Jones's oxidation. The mixture of epimeric carboxylic acids was treated with diazomethane and the corresponding methyl esters were separated by preparative TLC. Treatment of the crude 6-equatorial carboxamide (**22**), readily prepared from the corresponding acid, with thionyl chloride as the dehydration agent yielded crude **23**. After hydrolysis with potassium bicarbonate in aqueous methanol, **16ee** was obtained by column chromatography.

PMR Spectra

Since Hinckley's discovery of tris(dipivalomethanato)bis(pyridino)europium (III) [Eu(DPM)$_3$·Py$_2$] as a PMR shift reagent,[10] a number of workers have reported applications of the paramagnetic shifts induced by lanthanide complexes to structure determination of organic molecules having substituents with lone-pair electrons.[11] Demarco and coworkers[12] used Eu(DPM)$_3$ as a better shift reagent[13] to investigate the extent and potentials of such lanthanide-induced shifts in some fused ring systems such as steroids and triterpenes. We have successfully applied this method to obtain confirmatory evidence for the trans ring junction of 2α- and 2β-hydroxydecalins (**5e** and **5a**) prepared from **4e** and **4a**, respectively.

In the 100 MHz PMR spectra of **5a** and **5e** in CCl_4, only C_2-OH and C_2-H signals can be assigned, at δ 2.56 and 3.99 ppm in **5a**, and at δ 2.97 and 3.44 ppm in **5e**, respectively; the signals arising from the remaining protons show a hump ranging from δ 0.5 to 2.0 ppm. The spectra were then examined at various concentrations of Eu(DPM)$_3$. Upon an addition of 0.8 molar equivalent of Eu(DPM)$_3$ to the substrates, dramatic changes occurred in the spectra,as shown in Fig. 1. Signals were assigned on the basis of the magnitudes of their induced shifts expected from the McConnell and Robertson equation for the pseudo-contact shift[14] and the site of coordination,[11,12] their signal multiplicities, and spin-decoupling experiments. As expected, proton signals are shifted to lower fields in the order C_3-Heq, C_1-Heq, C_9-Hax, C_4-Hax, C_3-Hax, C_1-Hax, C_4-Heq, and C_{10}-Hax in **5a**, and in the order C_3-Hax, C_1-Hax, C_3-Heq, C_1-Heq, C_9-Hax≅C_4-Hax≅C_{10}-Hax, and C_4-Heq in **5e**. The signals of C_2-OH and C_2-H were not observed because they were shifted farther than 20 ppm[12] from Me_4Si as a lock-signal.

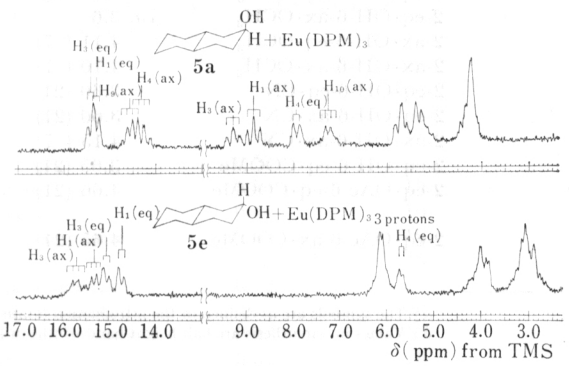


Fig. 1. PMR Spectra of 2β-and 2α-*trans*-decalols in CCl_4 containing Eu(DPM)$_3$ at 100 MHz

[Eu(DPM)$_3$]/[substrate] molar ratio=0.8

9) R. Greenwald, M. Chaykousky and E.J. Corey, *J. Org. Chem.*, **28**, 2742 (1964).
10) C.C. Hinckley, *J. Am. Chem. Soc.*, **91**, 5160 (1969).
11) C.C. Hinckely, M.R. Klotz and F. Patil, *J. Am. Chem. Soc.*, **93**, 2417 (1971); J.K.M. Sanders and D.H. Williams, *ibid.*, **93**, 641 (1971); J. Briggs, F.A. Hart, G.P. Moss and E.W. Randall, *Chem. Commun.*, 1971, 364; R.E. Rondeau and R.E. Sievers, *J. Am. Chem. Soc.*, **93**, 1522 (1971); and references cited therein.
12) P.V. Demarco, T.K. Elzey, R.B. Lewis and E. Wenkert, *J. Am. Chem. Soc.*, **92**, 5734, 5737 (1970).
13) J.K.M. Sanders and D.H. Williams, *Chem. Commun.*, **1970**, 422.
14) H.M. McConnell and R.E. Robertson, *J. Chem. Phys.*, **29**, 1361 (1958).

TABLE I. PMR Data on 2,6-Disubstituted-*trans*-decalin Derivatives in $CDCl_3$

Compounds[a]	Chemical shift (δ, ppm, downfield from Me_4Si)		
	C_2-H	C_6-H	Other H
2-eq·OH	3.60 (21)[b]		
2-ax·OH	4.12 (7)		
2-eq·OTs	4.44 (21)		2.43, 7.55 (OTs)
2-ax·OTs	4.80 (7)		2.43, 7.55 (OTs)
2-eq·OH-6-CO	3.70 (21)		
2-ax·OH-6-CO	4.18 (7)		
2-eq·OAc-6-CO	4.76 (21)		2.07 ($OCOCH_3$)
2-ax·OAc-6-CO	5.14 (7)		2.02 ($OCOCH_3$)
2-eq·$OCOCF_3$-6-CO	4.99 (21)		
2-ax·$OCOCF_3$-6-CO	5.36 (7)		
2-eq·OTs-6-CO	4.53 (21)		2.45, 7.57 (OTs)
2-ax·OTs-6-CO	4.86 (7)		2.45, 7.57 (OTs)
2-eq·OH-6-eq·C_6H_5	3.62 (21)	2.56 (21)	
2-eq·OTs-6-eq·C_6H_5	4.45 (21)	2.57 (21)	2.43, 7.55 (OTs)
2-eq·OTs-6-ax·C_6H_5	4.44 (21)	3.12 (10)	2.42, 7.55 (OTs)
2-eq·OH-6-eq·Cl	*ca.* 3.6	*ca.* 3.8	
2-eq·OH-6-ax·Cl	3.60 (21)	4.52 (7)	
2-ax·OH-6-eq·Cl	4.12 (7)	3.85 (21)	
2-ax·OH-6-ax·Cl	4.13 (7)	4.53 (7)	
2-eq·OH-6-eq·OCH_3	3.60 (21)	3.12 (21)	3.33 (OCH_3)
2-eq·OH-6-ax·OCH_3	*ca.* 3.6	3.50 (7)	3.29 (OCH_3)
2-ax·OH-6-eq·OCH_3	4.11 (7)	3.13 (21)	3.33 (OCH_3)
2-ax·OH-6-ax·OCH_3	4.10 (7)	3.50 (21)	3.29 (OCH_3)
2-eq·OH-6-eq·CN	3.60 (21)	2.47 (21)	
2-eq·OH-6-ax·CN	3.60 (21)	3.00 (7)	
2-ax·OH-6-ax·CN	4.15 (7)	3.00 (7)	
2-eq·OH-6-eq·COOMe	3.65 (21)	2.37 (21)	3.65 ($COOCH_3$)
2-eq·OAc-6-eq·COOMe	4.66 (21)	2.30 (21)	3.65 ($COOCH_3$), 2.00 ($OCOCH_3$)
2-eq·OAc-6-ax·COOMe	4.65 (21)	2.73 (7)	3.69 ($COOCH_3$), 2.00 ($OCOCH_3$)

a) The symbols are as defined in the introduction (footnote 3).
b) Values in parenthesis are half-height band widths in Hz.

TABLE II. Differences in Chemical Shift between Axial and Equatorial Protons attached to the Substituent Bearing C_2- or C_6-Atom of 2,6-Disubstituted-*trans*-decalin Derivatives, $\delta_{a,e}$, in $CDCl_3$

Substituent at C_2 or C_6	Compounds	$\delta_{a,e}$ (ppm)
OH	Ex. 2-OH	0.52 ± 0.3
OAc	2-OAc-6-CO	0.37
OTs	2-OTs	0.34
	2-OTs-6-CO	0.33
$OCOCF_3$	2-$OCOCF_3$-6-CO	0.87
Cl	2-OH-6-Cl	0.67 ± 0.1
OCH_3	2-OH-6-OCH_3	0.37 ± 0.1
CN	2-eq·OH-6-CN	0.53
CO_2Me	2-eq·OAc-6-CO_2Me	0.43
C_6H_5	2-eq·OTs-6-C_6H_5	0.55

The most relevant signals of the juncture protons, C_9-Hax and C_{10}-Hax, in **5a** do appear as quartets of triplets at δ 14.58 and 7.27 ppm, respectively; this fact clearly shows that compound **5a** is a *trans*-fused decalol and has an axial hydroxyl group. If **5a** were a *cis*-fused decalol, both signals of the juncture protons would appear as doublets of quintets.

In the PMR spectra of fixed substituted cyclohexane molecules, an axial proton resonates generally at a higher field than does its equatorial counterpart.[15-17] Further, the signal pattern of an axial proton attached to a substituent-bearing carbon atom has a larger value for its half-height band width (19—23 Hz) than has the corresponding equatorial proton (6—8 Hz).[15-17] On the basis of the above general features, the configurational assignment (axial or equatorial) of substituents at the C_2- and C_6-positions was determined for all derivatives prepared. Table I lists all the compounds examined and their 60 MHz PMR spectral data. The spectra were analysed generally by the first order approximation and there is no ambiguity in the signal assignment.

In Table II are shown the differences in the chemical shift between axial and equatorial protons, $\delta_{a\cdot e}$, attached to the substituent-bearing C_2- and C_6-atoms. As expected from the general rule mentioned above, the signal of an axial proton appears at a considerably higher field than that of an equatorial proton. Espectially, the $\delta_{a\cdot e}$ values for cyano and trifluoroacetoxy groups are markedly larger than those for the other groups. The $\delta_{a\cdot e}$ values[18-20] obtained from other alicyclic compounds in the absence of the strong shielding effects of other substituents are summarized in Table III.

TABLE III. Differences in Chemical Shift between Axial and Equatorial Protons in Alicyclic Compounds, $\delta_{a,e}$

Substituent	Compounds	$\delta_{a,e}$ (ppm)	Ref.
OH	*trans*-2-decalol	0.53	18
	10-methyl-*trans*-2-decalol	0.53	18
	4-*t*-butyl-cyclohexanol	0.56	19
	3-hydroxy-5α-cholestane	0.44	16
OAc	1-acetoxy-4-*t*-butylcyclohexane	0.51	19
	3-acetoxy-5α-cholestane	0.33	16
OTs	1-tosyloxy-4-*t*-butylcyclohexane	0.50	19
Cl	1-chloro-4-*t*-butylcyclohexane	0.71	20
OCH_3	1-methoxy-4-*t*-butylcyclohexane	0.38	19
CN	1-cyano-4-*t*-butylcyclohexane	0.37	19
	3-cyano-5α-cholestane	0.61	16
Ph	1-phenyl-4-*t*-butylcyclohexane	0.51	20
	3-phenyl-5α-cholestane	0.63	7

Both half-height band widths and $\delta_{a\cdot e}$ value obtained for the present compounds demonstrate that the configurational assignments for the substituents are all correct.

Kawazoe and co-workers[17] found that there are characteristic differences in downfield shifts of signals of protons attached to carbon atoms bearing a hydroxy group due to acetylation of the hydroxyl group. Tori and Komeno[16] also studied the changes in chemical shifts of the protons attached to hydroxy or mercapto bearing carbon atoms due to acetylation. This shift has been called the acetylation shift.

15) N.C. Franklin and H. Felthamp, *Angew. Chem. Intern. Ed. Engl.*, **4**, 774 (1965).
16) K. Tori and T. Komeno, *Tetrahedron*, **21**, 309 (1965).
17) Y. Kawazoe, Y. Sato, T. Okamoto and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **11**, 328 (1963).
18) J.I. Musher, *J. Am. Chem. Soc.*, **83**, 1146 (1961).
19) E.E. Eliel and M.H. Gianni, *Tetrahedron Letters*, **1962**, 97.
20) L.M. Jackmann and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd Ed., Pergamon Press, New York, N.Y., 1969, p. 238.

In Table IV are shown our results for the acylation shifts of an axial and an equatorial hydroxyl group ($\delta_{OAc,OH}$, $\delta_{OCOCF_3,OH}$, $\delta_{OTs,OH}$). These results indicate that an axial proton is more deshielded than an equatorial proton by acylation, and that the magnitude of the shifts depends upon the difference in the degree of freedom of rotation of substituents.

Table IV. Acylation Shifts of the Proton attached to Hydroxy Bearing Carbon Atoms, $\delta_{OAc,OH}$, $\delta_{OCOCF_3,OH}$ and $\delta_{OTs,OH}$ (in ppm)

Compounds	$\delta_{OAc,OH}$	$\delta_{OCOCF_3,OH}$	$\delta_{OTs,OH}$
2-eq·OH (2-ax·H)	—	—	0.84
2-ax·OH (2-eq·H)	—	—	0.68
2-eq·OH-6-CO (2-ax·H)	1.06	1.29	0.83
2-ax·OH-6-CO (2-eq·H)	0.96	1.18	0.68
2-eq·OH-6-eq·OCH_3 (2-ax·H)	—	—	0.83
2-eq·OH-6-eq·CO_2Me (2-ax·H)	1.01	—	—

The PMR spectral data listed in the Table (I—IV) may be applied to structure estimation of rigid alicyclic compounds with one axial and one equatorial substituent.

IR Spectra

In alicyclic systems, there is a rule that the C-OH stretching vibration for an axial hydroxyl group is at a higher wave length than that for the corresponding equatorial hydroxyl group.[5] Clarke and Martin[5] have made a detailed IR spectroscopic investigation of the axial and equatorial character of the hydroxyl group in *cis* and *trans*-fused decalols. They established a relationship between the spectra and conformations (axial and equatorial), and showed that an axial and an equatorial C-OH stretching vibration in *trans*-decalin systems indicates peaks at 1004—1011 cm^{-1} and 1017—1042 cm^{1-}, respectively.

The relative configuration of the hydroxyl group in all compounds in this study was also determined on the basis of the wave length of the C-OH stretching vibration. These data are given in Table V.

Table V. IR Data on 2,6-Disubstituted-*trans*-decalin Derivatives in CS_2

Compounds	C_2-Atom		C_6-Atom
	ν_{C-OH}	ν_{OH}	$\nu_{substituent}$
2-ax·OH	1005	3611	
2-eq·OH	1025, 1038	3605	
2-ax·OH-6-CO	1001	3604	1713 (C=O)
2-eq·OH-6-CO	1026 (s), 1039 (w)	3601	1713 (C=O)
2-ax·OH-6-ax·OCH_3	1002	3614	2815 (OCH_3)
2-ax·OH-6-eq·OCH_3	1009	3616	2815 (OCH_3)
2-eq·OH-6-ax·OCH_3	1037	3607	2817 (OCH_3)
2-eq·OH-6-eq·OCH_3	1033	3603	2815 (OCH_3)
2-ax·OH-6-ax·Cl	997	3610	718 (Cl)
2-ax·OH-6-eq·Cl	1001	3615	750, 763 (Cl)
2-eq·OH-6-ax·Cl	1025 (w), 1035 (s)	3604	722 (Cl)
2-eq·OH-6-eq·Cl	1030	3607	751, 763 (Cl)
2-ax·OH-6-ax·CN	1001	3610	2236 (C≡N)
2-eq·OH-6-ax·CN	1037	3600	2235 (C≡N)
2-eq·OH-6-eq·CN	1038	3608	2240 (C≡N)
2-eq·OH-6-eq·COOMe	1012, 1037	3604	1736 (CO_2CH_3)
2-eq·OAc-6-ax·COOMe	1025 (s), 1036 (w)		1735 (CO_2CH_3)
2-eq·OAc-6-eq·COOMe	1028		1736 (CO_2CH_3)

Experimental[21]

2α- and 2β-Hydroxy-*trans*-6-decalones (4e and 4a)——Compounds (**4e** and **4a**) were prepared from 6-methoxy-2-tetralol by the procedure of Clark and Martin.[5] **4e**, mp 83—85° (lit.[5] mp 82—84.5°); **4a**, mp 83.5—86.0° (lit.[5] mp 81—86°). These compounds (**4a** and **4e**) were identical with authentic 2α- and 2β-*trans*-decalins in every respect.

2α- and 2β-Hydroxy-*trans*-decalins (5e and 5a)——A mixture of **4e** (2.0 g), diethylene glycol (40 ml), 85% KOH pellets (4.8 g), and $NH_2NH_2 \cdot 2H_2O$ (2.0 ml) was refluxed at 110—120° (bath temp.) for 2.5 hr. The condenser was removed to allow the aqueous liquor to evaporated and the temperature to rise to about 200°. After refluxing at the same temperature for about 3.5 hr, the mixture was cooled and diluted with water. The white precipitate which formed was filtered, washed with water, and dried (P_2O_5) giving 1.5 g of product **5e**. Recrystallization from *n*-hexane afforded 1.46 g, mp 72—74° (lit.[22] mp 75°). *Anal.* Calcd. for $C_{10}H_{16}O$: C, 77.86; H, 7.74. Found: C, 77.81; H, 11.72.

5a was prepared from **4a** by the same procedure. mp 50.5—52.0° (lit.[22] mp 53°). *Anal.* Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.62; H, 11.69.

2α-Hydroxy-*trans*-decalin-6-ethylene Ketal (6e)——To a stirred solution of **4e** (4.0 g) in abs. THF (40 ml) was added ethylene glycol (20 ml) and BF_3 etherate (*ca.* 1 ml) and the mixture was left to stand at room temperature over night. The mixture was poured into Na_2CO_3 (14 g) in H_2O (200 ml) and extracted with ether. The ether extracts were washed with satd. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give residual oil which was recrystallized from ether–*n*-hexane to furnish 4.77 g, mp 83—86° of **6e**. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3616 (OH), 1031 (C-OH).

2β-Hydroxy-*trans*-decalin-6-ethylene Ketal (6a)——Compound (**6a**) was obtained from **4a** by the procedure already described. mp 47—51°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3622 (OH), 1007 (C-OH).

2β-Methoxy-*trans*-decalin-6-ethylene Ketal (7e)——Sodium hydride (2.74 g, 50% dispersion in mineral oil) contained in a flask was washed with abs. petroleum ether to remove the mineral oil. The system was then alternately evacuated and filled with Ar gas. DMSO (35 ml) was introduced *via* a dropping funnel and the mixture was stirred at 75—85° for *ca.* 45—60 min. About 18 ml of methyl sulfinyl carbanion solution was added to a solution of **6e** (4.0 g) in DMSO (20 ml). The mixture was stirred under an Ar stream for 20 min at room temperature. MeI (9.0 g) was added to the mixture which was then stirred for another 1 hr. The resulting solution was pured into H_2O (175 ml) and extracted with ether. The ether extracts were washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 4.36 g of crude **7e**. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2816 (OCH_3).

2α- and 2β-Hydroxy-6β-methoxy-*trans*-decalins (9ee and 9ae)——Crude **7e** (3.26 g) was dissolved in 75% AcOH (25 ml) and the solution was heated at 75—80° for 2 hr then left to stand at room temperature over night. Water (*ca.* 100 ml) was added to the solution which was then extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with aqueous $NaHCO_3$ and with water then dried over anhyd. Na_2SO_4 to give 3.57 g of crude **8e**. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2815 (OCH_3).

To a stirred solution of lithium tri-*t*-butoxy aluminium hydride (10.5 g) in abs. THF (60 ml) crude **8e** (3.57 g) in abs. THF (30 ml) was added dropwise at 0—7° and the mixture was stirred at 0—10° for 5 hr. About 1.5 ml water in ether was added under cooling to the stirred mixture and stirring was continued for another 30 min. The resulting solution was filtered and the filtrate was washed with 1N HCl and with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 3.38 g of crude **9ee** and **9ae**. GLC analysis on a column of carbowax 20M on 100/120 mesh Gaschrom Q indicated that the residual oil was a mixture of **9ee** and **9ae** in a 87:13 ratio. Recrystallization from ether–*n*-hexane afforded 2.43 g, mp 86—88° of pure **9ee**. *Anal.* Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.73; H, 10.90.

9ae was isolated and purified from the mother liquor by preparative TLC, colorless oil (210 mg, $n_D^{26.3}$ 1.4887). *Anal.* Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.73; H, 10.90.

2α- and 2β-Hydroxy-6α-methoxy-*trans*-decalins (9ea and 9aa)——Compounds (**9ea** and **9aa**) were prepared from **7a** (4.39 g) by the above mentioned method. GLC analysis showed that the reaction product was a mixture of **9ea** and **9aa** (88:12). The epimeric alcohols were separated by column chromatography followed by preparative TLC. **9ea** (3.82 g, colorless oil, GLC pure, $n_D^{26.0}$ 1.4880) and **9aa** (230 mg, colorless oil, GLC pure, $n_D^{25.5}$ 1.4898) were obtained. **9ea**, *Anal.* Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.97; H, 10.84. **9aa**, *Anal.* Found: C, 71.63; H, 10.96.

---

21) Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. The IR spectra were determined with a Nippon Bunko DS201B spectrometer. The PMR spectra were taken with Varian A-60 and/or an HA-100 spectrometer using tetramethylsilane as an internal standard and the tabulated in the order; chemical shift (δ, ppm downfield from TMS), proton number, multiplicity (s=singlet, br.s=broad singlet), half-height band width, and assignment (ax·H=axial proton, eq·H=equatorial proton) of protons. Column, thin layer, and preparative TLC were carried out with Kieselgel, 0.2—0.5 mm (Merck), Kiesel gel GF_{254} nach Stahl (Merck), and Kiesel gel G nach Stahl (Merck), respectively.

22) W. Hückel, *Ann.*, **441**, 31 (1925).

2α-Hydroxy-6-phenyl-6-hydroxy-*trans*-decalin (10)——To a stirred mixture of Mg turnings (3.04 g), a crystal of I_2, and abs. THF (50 ml) was added C_6H_5Br (19.63 g) in abs. THF (80 ml) and the mixture was stirred at 40—70° for 30 min then allowed to stand for 2 hr at 55—60°. Upon completion of Grignard reagent formation, **4e** (3.5 g) in abs. THF (100 ml) was added dropwise over 20 min at 45—50° and the mixture was refluxed for 6 hr. The mixture was then left to stand at room temperature over night. The mixture was cooled in ice–water and the addition compound was decomposed by adding 25% NH_4Cl (100 ml) dropwise with stirring. The mixture became clear and the salt separated as a cake. The resulting solution was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give crude crystals of a mixture of two compounds, 6β-hydroxyl-6α-phenyl- and 2α,6α-dihydroxy-6β-phenyl-*trans*-decalins, in an approximately 56: 44 ratio (GLC analysis of their acetates). The crystals were recrystallized from acetone to furnish 2.44 g, mp 165—167°, IR ν_{max}^{Nujol} cm^{-1}: 699, 720, 740, 763, 770 (Ph), 1001, 1015 (C–OH). The mother liquor was recrystallized from acetone–*n*-hexane to furnish 1.518 g, mp 165—171°.

2α-Hydroxy-6α-phenyl- and 6β-Phenyl-*trans*-decalins (11ea and 11ee)——A mixture of crude **10** (2.83 g), W-2 Raney nickel (85 g), and EtOH (300 ml) was stirred for 3.0 hr then the Raney nickel was filtered off. Evaporation of the EtOH *in vacuo* (<30°) gave crude crystals of a mixture of **11ea** and **11ee**, which were recrystallized from ether–*n*-hexane to afford 1.28 g, mp 129—133°, and a residual oil 1.12 g. GLC analysis indicated that the first crystals and the residual oil were mainly **11e**, and **11a**, respectively. Further recrystallization of the crystals gave pure **11ee**, mp 132—134°. *Anal.* Calcd. for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.66; H, 9.60.

The crude oil **11a** was tosylated with *p*-TsCl in dry pyridine. Pure tosylate was obtained by elution chromatography on silica gel in ether–*n*-hexane, followed by twice recrystallization from ether–*n*-hexane, mp 92—94°. IR $\nu_{max}^{CS_2}$ cm^{-1}: 787, 726, 700 (Ph), 1369, 1179 (OTs). *Anal.* Calcd. for $C_{23}H_{28}O_3S$: C, 71.85; H, 7.33, S, 8.34. Found: C, 72.00; H, 7.43; S, 8.42.

2β-Chloro-*trans*-6-decalone (12a)——To a stirred solution of **6e** (4.53 g) in abs. $CHCl_3$ (250 ml) containing dry $CaCO_3$ (9.53 g) in suspension, freshly sublimed PCl_5 (4.50 g) was added portionwise over 1 hr at −1——4°. The mixture was stirred for a further 1 hr at −3——4°. $NaHCO_3$ solution (*ca.* 300 ml) was then added dropwise under cooling and the mixture was left to stand at 10° for 1 hr. The organic and aqueous layers were separated and the aqueous layer was extracted with ether. The ether extracts and the organic layer were combined and washed with 2N Na_2CO_3 and with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 4.92 g of residual oil which was dried by dissolving in C_6H_6 and evaporating the solvent.

To a solution of the dried residual oil (4.92 g) in THF (80 ml) 3N $HClO_4$ (32 ml) was added dropwise and the mixture was stirred ar toom temperature for 4 hr. The mixture was then diluted with H_2O (200 ml) and extracted with ether. The ether extracts were washed with 1N KOH and with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 3.67 g of residual oil. The oil was chromatographed on neutral silica gel (Merck). The major compound **12a** (3.13 g) was obtained in the fractions eluated with 4: 1—1: 1 of petr. ether: C_6H_6. IR $\nu_{max}^{CS_2}$ cm^{-1}: 722 (Cl), 1720 (C=O).

2α-Hydroxy- and 2β-Hydroxy-6α-chloro-*trans*-decalins (13ea and 13aa)——Compounds (**13ea and 13aa**) were prepared from **12a** with lithium aluminum tri-*t*-butoxy hydride by the procedure described above. GLC analysis showed that the ratio of reaction products (**13ea** and **13aa**) was 91.5/8.5. **13ea** was purified by twice recrystallization from ether–*n*-hexane, mp 105—107°. *Anal.* Calcd. for $C_{10}H_{17}OCl$: C, 63.65; H, 9.08; Cl, 18.79. Found: C, 63.80; H, 9.11; Cl, 18.90. **13aa** was isolated from mother liquor by preparative TLC and purified by recrystallization from *n*-pentane–ether, mp 88—89°. *Anal.* Calcd. for $C_{10}H_{17}OCl$: C, 63.65; H, 9.08; Cl, 18.79. Found: C, 63.91; H, 9.14; Cl, 18.88.

2α-Chloro-*trans*-6-decalone (12e)——To a stirred solution of **6a** (6.80 g) in abs. $CHCl_3$ (500 ml) containing dry $CaCO_3$ (16.3 g) in suspension, freshly sublimed PCl_5 (7.34 g) was added portionwise over 1 hr at −11——12° and the mixture was stirred at −9——4° for 1 hr, then at −4——0° for 35 min. Sat. $NaHCO_3$ was then added dropwise to the mixture at below 10° and stirring was continued at 7—15° for 85 min. The resulting solution was worked up in the usual manner. GLC analysis indicated that the reaction product consisted mainly of two compounds, olefin (48%) and **12e** (46%), plus a minor amount of unreacted starting material (6%). Column chromatography on neutral silica gel (Merck), afforded 1.89 g of **12e**. IR $\nu_{max}^{CS_2}$ cm^{-1}: 1723 (C=O), 756 (C_6H_5).

2α-Hydroxy- and 2β-Hydroxy-6β-chloro-*trans*-decalin (13ee and 13ae)——Compounds (**13ee** and **13ae**) were prepared from **12e** (1.83 g) with lithium aluminum tri-*t*-butoxy hydride. The reaction product was recrystallized from ether–*n*-pentane to afford 1.29 g, mp 88.0—89.5° of **13ee**. *Anal.* Calcd. for $C_{10}H_{17}OCl$: C, 63.65; H, 9.08; Cl, 18.79. Found: C, 63.64; H, 9.38; Cl, 19.00. From the mother liquor, **13ae** (0.36 g) was isolated by preparative TLC and purified by recrystallization from *n*-pentane, mp 82.5—83.5°. *Anal.* Calcd. $C_{10}H_{17}OCl$: C, 63.65; H, 9.08; Cl, 18.79. Found: C, 63.57; H, 9.13; Cl, 18.79.

2β-Cyano-*trans*-6-decalone (15a)——A mixture of **14e** (5.72 g, mp 80—84°), dried NaCN (4.28 g), abs. N-methyl-2-pyrrolidone (400 ml), and *t*-BuOH (20 ml) was heated at 91—95° for 24 hr with stirring. The mixture was cooled and poured into H_2O (1.6 liter) and extracted into ether. The ether extracts were washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 3.35 g of oily products, which were chromatographed on neutral silica gel (Merck) in C_6H_6–$CHCl_3$. Olefin (0.40 g) was collected in the fractions eluted with C_6H_6. The solvent was then changed to 4: 1—1: 1 C_6H_6–$CHCl_3$ and **15a** (1.45 g) was eluted. The

crude **15a** was recrystallized from ether *n*-pentane to furnish 1.30 g, mp 96.0—99.0°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2236 (C≡N), 1717 (C=O). PMR ($CDCl_3$): δ 3.02 (1H, br s, $W1/2=7$ Hz, 6-eq·H).

2α-Hydroxy- and 2β-Hydroxy-6α-cyano-*trans*-decalins (16ea and 16aa)——Compounds (**16ea** and **16aa**) were obtained from **15a** by reduction with LiAlH $(OC_4H_9)_3$ or $NaBH_4$ as described above. GLC analysis showed that the reduction product ratio (**16ea/16aa**) with the two reducing reagents was 8/92, 19/81, respectively.

The crude reduction product was chromatographed in ether–*n*-hexane on neutral silica gel (Merck). Both the minor (**16aa**, 61 mg) and major (**16ea**, 1.4 g) components were eluated with ether–*n*-hexane (2: 1). Pure **16aa** was obtained by twice recrystallizing from ether–*n*-pentane, mp 93—95°. *Anal.* Calcd. for $C_{11}H_{17}ON$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.49; H, 9.30; N, 7.83. **16ea** was purified by recrystallization from ether to afford 1.36 g, mp 58—60°. *Anal.* Calcd. for $C_{11}H_{17}ON$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.93; H, 9.42; N, 8.10.

2α-Acetoxy-6-methoxymethylene-*trans*-decalin (18)——Sodium hydride (7.25 g, 50% dispersion in mineral oil) was washed three times with abs. pet. ether and dried *in vacuo*. The flask was filled with Ar gas and abs. DMSO (100 ml) was added *via* a dropping funnel. The mixture was heated at 70—75° for *ca.* 50 min. The resulting solution was cooled with ice–water and methoxymethyl triphenylphosphonium chloride (46.7 g) in warm DMSO (160 ml) was added to the solution. The resulting darked red soultion was stirred under Ar gas at room temperature for 10 min. To this solution of methoxymethylene triphenyl phosphorane was added 6α-acetoxy-*trans*-2-decalone (14.21 g) in abs. THF (60 ml) at 19—33° and the mixture was stirred under argon gas at 25—35° for 3.5 hr. The mixture was poured into H_2O (*ca.* 800 ml) and extracted with *n*-hexane–ether (2: 1). The extracts were washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give *ca.* 26 g of residual oil, which was again acetylated with Ac_2O in pyridine and worked up in the usual manner. The resulting oil was chromatographed in *n*-hexane–C_6H_6 on neutral silica gel. **18** was collected in the fractions eluted with C_6H_6–$CHCl_3$ (2: 1—1: 1). IR $\nu_{max}^{CS_2}$ cm^{-1}: 2827, 1690, 1133, 1105, 1076 (enol ether), 1737, 1240 (OAc), 1026 (C-OAc). PMR ($CDCl_3$): δ 2.00 (3H, s, $OCOCH_3$), 3.52 (3H, s, OCH_3), 4.73 (1H, br s, $W1/2=21$ Hz, 2-ax·H), 5.75 (1H, br s, >C=CH–).

2α-Acetoxy-*trans*-decalin-6α-carboxylic- and 6β-carboxylic Acid (20a and 20e)——To a stirred solution of crude **18** (7.25 g) in CH_2Cl_2 (180 ml) was added ether saturated with 70% $HClO_4$ (*ca.* 50 ml) and the mixture was at room temperature for 1 hr. To this mixture, sat. $NaHCO_3$ was added slowly with stirring. The resulting solution was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 7.16 g of residual oil.

To a solution of the residual oil in pure acetone (400 ml) standard CrO_3 reagent (*ca.* 16—17 ml) was added rapidly at 7—12° with vigorous stirring under Ar gas. After addition of Jones's reagent, the reaction temperature was maintained at 20—23° for 1 hr. The mixture was diluted with H_2O (*ca.* 2 liter) and the precipitate formed was filtered, giving 4.10 g of crude product. The aqueous layer was reduced *in vacuo* and the residue was extracted with ether. The ether extracts were washed with aqueous $NaHCO_3$ and the washings were acidified with 3N HCl. The precipitate which formed was filtered and dried over P_2O_5 *in vacuo*, giving 1.34 g, mp 138—155° (**20a**: **20e**=27 : 73, by GLC analysis). The crude product was recrystallized from ether–*n*-hexane to afford 2.27 g, mp 169—171° (**20e**, GLC pure). Further recrystallization from ether–*n*-hexane gave a melting point of 170—171°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3100—2500 (broad), 1709 (COOH), 1741, 1240 (OAc). PMR ($CDCl_3$): δ 2.00 (3H, s, $OCOCH_3$), 2.35 (1H, br s, $W1/2=21$ Hz, 6-ax·H), 4.74 (1H, br s, $W1/2=21$ Hz, 2-ax·H), 10.47 (1H, br s, COOH). *Anal.* Calcd. for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.70; H, 8.43. The mother liquor was dissolved in ether and the solution was worked up as described above, giving 0.707 g, mp 161—165° (**20e**: **20a**=97: 3, by GLC analysis).

Methyl 2α-acetoxy-*trans*-decalin-6α- and 6β-carboxylate (21a and 21e)——To a stirred solution of crude epimeric carboxylic acid (1.34 g) in ether (50 ml) was added excess ethereal CH_2N_2 at room temperature and the mixture was stirred at room temperature for 2 hr. The solvent and excess reagent were romoved first at atmospheric pressure then *in vacuo*, giving 1.48 g of residual oil. The oil crystallized directly on standing. The methyl esters were separated by preparative TLC and purified by recrystallization from ether–*n*-pentane. **21a**, mp 73—74°. *Anal.* Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 66.03; H, 8.70. **21e**, mp 90.5—92.5°. *Anal.* Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 66.24; H, 8.45.

2α-Acetoxy-*trans*-decalin-6β-carboxamide (22)——To a stirred solution of pure **20e** (1.78 g) in abs. C_6H_6 (20 ml), $SOCl_2$ (*ca.* 5 ml) was added slowly and the mixture was stirred at room temperautre for 5 hr. The solvent was removed as far as possible *in vacuo*, leaving a residual oil. A solution of the crude acid chloride in C_6H_6 (60 ml) was cooled and saturated with NH_3. The mixture was stirred for 10—15 min and dissolved in AcOEt (400 ml). The solution was washed with sat. $NaHCO_3$ and with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give crude crystals. The crystals were acetylated with Ac_2O in pyridine and worked up in the usual manner to give 1.43 g of crude **22**. mp 183—188°. IR ν_{max}^{KBr} cm^{-1}: 1657, 1627, 3256, 3280 ($CONH_2$), 1740, 1250, 1238 (OAc), 1031 (C-OAc).

2α-Acetoxy-6β-cyano-*trans*-decalin (23)——Crude **22** (1.43 g) was dissolved in $SOCl_2$ (*ca.* 5 ml) and refluxed for 1 hr. Excess $SOCl_2$ was evaporated *in vacuo*. The oil was dissolved in ether and the ether solution was washed with sat. $NaHCO_3$ and with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give a crude oil, which was chromatographed on neutral silica gel (Merck) then recrystallized from *n*-pentane

to afford 1.17 g, mp 70—72°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2242 (C≡N), 1730, 1255 (OAc), 1031 (C-OAc). PMR ($CDCl_3$): δ 2.00 (3H, s, $OCOCH_3$), 2.41 (1H, br s, $W1/2=21$ Hz, 6-ax·H), 4.71 (1H, br s, $W1/2=21$ Hz, 2-ax·H).

6β-Cyano-2α-hydroxy-*trans*-decalin (16ee)——To an aqueous solution of $KHCO_3$ (1 g) in H_2O (30 ml) was added **23e** (1.07 g) in MeOH (30 ml). The mixture was refluxed for 2 hr then the solvent was removed as far as possible *in vacuo*. The residual oil was dissolved in CH_2Cl_2 and the solution was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 0.924 g of crude product. The oil was chromatographed twice on neutral silica gel in C_6H_6–AcOEt and purified by recrystallization from ether–*n*-pentane to afford 0.728 g, mp 44—47° of pure **16ee**. *Anal.* Calcd. for $C_{11}H_{17}ON$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.66; H, 9.75; N, 7.86.

2α-Hydroxy-*trans*-decalin-6β-carboxylic Acid (24)——A solution of KOH (4.0 g) in H_2O (50 ml) was added slowly to **20e** (2.25 g) in MeOH (30 ml) with cooling and the mixture was stirred at 30° for 2 hr. Solvent was removed as far as possible *in vacuo* then water added. The mixture was acidified with dil. HCl under cooling. The carboxylic acid which separated as a solid was filtered and dried (P_2O_5) *in vacuo*, giving 1.80 g, mp 204—206°. After recrystallization from AcOEt, it melted at 208—209°. IR ν_{max}^{KBr} cm^{-1}: 3150—2600 (broad), 1709 (COOH), 3430 (OH), 1029 (C-OH), *Anal.* Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.87; H, 9.14.

Methyl 2α-Hydroxy-*trans*-decalin-6β-carboxylate (25)——To a stirred solution of **24e** (1.75 g) in MeOH (20 ml) excess ethereal CH_2N_2 was added slowly and the mixture was stirred at room temperature for 2—3 hr. When reaction was completed, the mixture was worked up in the usual manner. The crude product was recrystallized from ether–*n*-pentane to furnish 1.47 g, mp 90—92° of pure **25e**. *Anal.* Calcd. for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.66; H, 9.44.

Gas Liquid Chromatographic Analysis——Analyses were carried out on a Hitachi gas chromatograph Model K53 equipped with a hydrogen flame ionization detecter using the following columns: 1 m×3 mm or 2 m×3 mm stainless steel coulmn packed with (A) 5% Carbowax 20M or 10% Carbowax 20M; (B) 5% XE-60; (C) 5% SE-30; (D) 5% QF-1 on Gaschrom Q (100—120 mesh). Nitrogen was used as a carrier gas.

Acknowledgement The authors wish to express their deep gratitude to prof. Y. Tamura, University of Osaka, for his helpful discussions. Thanks are also due to Dr. K. Tori of this laboratory for his valuable discussion on the PMR study.