Chem. Pharm. Bull. 29(11)3238—3248(1981)

4,4-Dimethyl Effect (2).[1,2] Syntheses, ^{1}H- and ^{13}C-Nuclear Magnetic Resonance Spectra, and the Conformations of 6α- and 6β-Substituted-1,1,10β-trimethyl-*trans*-decal-2-ones (8α- and 8β-Substituted-4,4,10β-trimethyl-*trans*-decal-3-ones), Models of 4,4-Dimethyl-steroid- and Triterpenoid-3-ketones[3]

Yoshisuke Tsuda,* Kimihiro Yoshimoto, Takeshi Yamashita, and Miyuki Kaneda[4]

Faculty of Pharmaceutical Sciences, Kanazawa University, 13-1 Takara-machi, Kanazawa 920, Japan

(Received May 15, 1981)

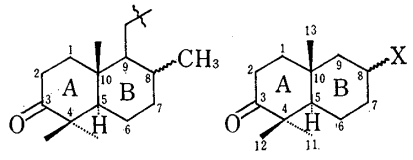
A set of 6α- and 6β-(hydroxy, acetoxy, and *p*-bromobenzoyloxy)-1,1,10β-trimethyl-*trans*-decal-2-ones was synthesized in an unequivocal manner, and the ^{1}H-nuclear magnetic resonance (NMR) spectra, TH effect (ASIS shift on continuously changing the solvent from chloroform-*d* to benzene-d_6), and ^{13}C-NMR spectra of these compounds are discussed in relation to the conformations of ring A. In solution, ring A of the 6β-derivatives was shown to be more distorted (flattened) than that of 6α-derivatives. This was also true in the crystalline state as determined by X-ray analyses of their *p*-bromobenzoates. The TH effect was found to reflect sensitively small conformational changes in ring A.

Keywords——1,1,10β-trimethyl-6α-substituted-*trans*-decal-2-ones; 1,1,10β-trimethyl-6β-substituted-*trans*-decal-2-ones; 6β-hydroxy-5,5,9β-trimethyl-*trans*-decal-2-one; conformational analysis; transmission of steric compression; ^{13}C-NMR; ^{1}H-NMR; TH effect; ASIS shift; X-ray analysis

In a previous paper,[2] we showed that the "4,4-dimethyl effect" together with its anomalies also occurs in a bicyclic system such as an onoceranoid (**1**); the Cotton effect of the 3-ketone changes its sign depending on the stereochemistry of the C_8-methyl group.[5]

Such a change appears to reflect the conformational changes caused by configurational changes of a substituent X in a simple system such as **2**.[6]

In the present investigation, unequivocal syntheses of the 8α- and 8β-hydroxy derivatives of **2** are described and the transmission of the steric compression caused by an 8β-substituent to ring A is discussed in relation to ^{1}H- and ^{13}C-nuclear magnetic resonance (NMR) spectra, and their ASIS shift.



1 **2**

Chart 1

Syntheses

The key intermediate, 3β-hydroxy-4,4,10-trimethyl-*trans*-decal-8-one (**11**),[6] has already been described by Halsall *et al.*,[7] and Narang and Dutta.[8] We have prepared it in a different way.

Michael addition of **3**[9] with methyl vinyl ketone followed by aldol condensation with a catalytic amount of pyrrolidine-acetic acid provided the bicyclic enone (**4**) in 87% yield.[10] Treatment of **4** with *t*-BuOK and excess CH_3I afforded the dimethyl derivative (**5**) in 83% yield. $NaBH_4$ reduction of **5** in hot methanol[11] gave, with concomitant lactonization, the lactone (**6**) in 88% yield. The same lactone (**6**) was obtained in 87% yield by catalytic hydrogenation of **5** in ethanol over PtO_2.[12] Reduction of **6** with $LiAlH(OBu\text{-}t)_3$ in tetrahydrofuran yielded the crystalline lactol (**7**) (73% yield).

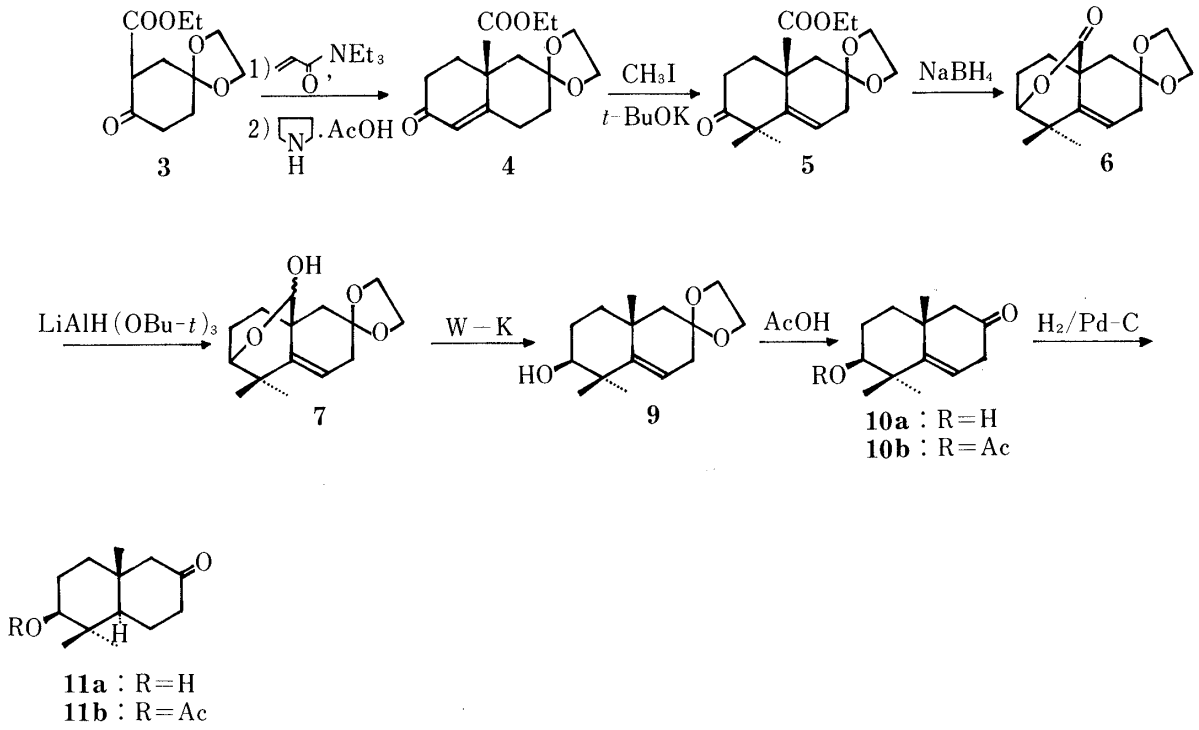


Chart 2

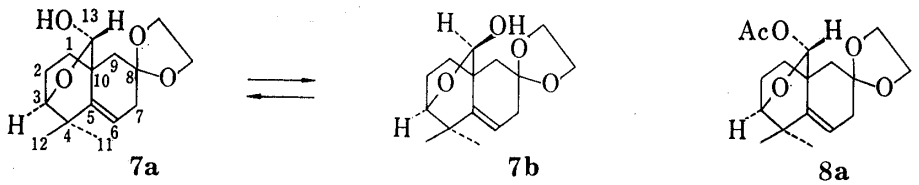
An interesting epimerization of this lactol was observed. The lactol showed the ^{1}H-NMR spectrum of a single compound (**7a**), but on standing for 24 h in $CDCl_3$ it changed into an approximately 1 : 1 mixture of two epimers (**7a** and **7b**). Removal of the solvent by evaporation left a crystalline residue which again showed the spectrum of a single compound corresponding to **7a**. In agreement with the ^{1}H-NMR evidence, the ^{13}C-NMR spectrum of the lactol, when measured immediately after dissolution of the compound, gave peaks corresponding to only **7a**, but gave peaks due to a mixture of **7a** and **7b** after 24 h. The stereochemistries of **7a** and **7b** were elucidated as follows. In the ^{13}C-NMR spectra, the hemiacetal carbon (C-13) of **7a** appears at higher field by 1.9 ppm than that of **7b** suggesting that its hydroxy group has axial orientation,[13] and the C-5 signal (γ-position relative to OH) of **7b** resonates at higher field (2.6 ppm) than that of **7a**, showing that C-5 of **7b** is more sterically compressed.[13] The ^{1}H-NMR signal of one of the methyls (H-12) in **7b** was shifted downfield by 0.13 ppm from that of **7a**, showing the presence of a space-directing effect of the hydroxyl group to H-12. All of the above findings indicate that the OH group in **7b** is on the same side as C-5 and H-12. The hemiacetal proton (H-13) of **7a** showed a W-type long-range coupling of *ca.* 1 Hz (with 1α-H) in addition to the coupling with the OH group. Such a long-range coupling was not observed in **7b**.

Kinetic acetylation of **7a** with Ac_2O–pyridine gave the single acetate (**8a**), the configuration of which was deduced from the acylation shift value of the hemiacetal moiety.[14] McQuillin and Yeates[11] obtained the analogous lactol (**13**) in 85% yield by reduction of the lactone (**12**) with lithium triethoxyaluminum hydride, but with no indication of the orientation of the lactol hydroxy-group, though the product appeared to be a single isomer.

Wolf-Kishner reduction of **7** under forcing conditions[15] gave the trimethyl derivative (**9**) in 65% yield. Since **9** was resistent to catalytic hydrogenation, the ethyleneacetal was first hydrolyzed by 80% AcOH to yield **10a**, which was then hydrogenated over Pd–C to provide the saturated ketone (**11a**), mp 116—118°C (53% yield). This gave the acetate (**11b**), mp 110—112°C.

Halsall *et al.*[7] reported that hydrogenation of **10a** with Pd–C in EtOH or AcOH gave the *trans*-decalone (**11a**) (mp 144—145°C, sublim. at 115°C; acetate **11b**, mp 113°C), while

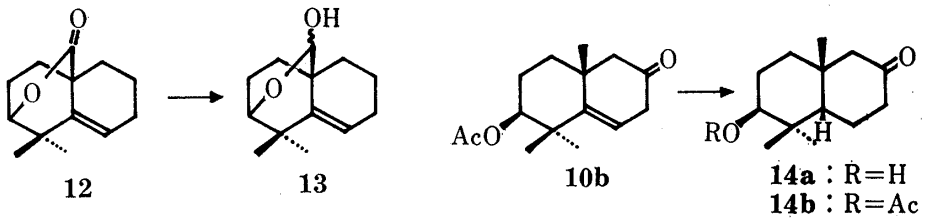
TABLE I. ^{1}H- and ^{13}C-NMR Spectra of the Lactols **7a**, **7b**, and the Acetate **8a**[a]



7a **7b** **8a**

Position	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
1	22.7[c]		22.7[c]		22.3[c]	
2	23.1[c]		23.0[c]		24.5[c]	
3	77.7	3.50 t, J=2.5 Hz	77.6	3.49 t, J=2.5 Hz	78.1	3.56 t, J=2.5 Hz
4	38.9		38.7		39.0	
5	146.7		144.1		145.5	
6	116.8	5.52 t, J=4.2 Hz	119.1	5.66 t, J=4.2 Hz	117.7	5.56 t, J=4.2 Hz
7	35.3	2.28 d, J=4.2 Hz	35.1	2.28 d, J=4.2 Hz	35.3	2.28 d, J=4.2 Hz
8	107.9		107.9		107.5	
9	37.9		37.9		37.8	
10	40.4		41.1		39.2	
11	27.4	1.06 s	27.7	1.06 s	27.4	1.08 s
12	28.6	1.18 s	28.2	1.31 s	28.5	1.21 s
13	96.1	5.14 d,[b] J=4.4 Hz	98.2	4.90 d, J=6.6 Hz	95.9	6.08 d, J=1.2 Hz
OH		3.78 d, J=4.4 Hz		4.34 d, J=6.6 Hz		
Ethylene acetal	64.1	3.93 s	64.3	3.97 s	64.2	3.92 s
Ac					21.4	2.10 s

a) Solvent, $CDCl_3$. δ ppm from TMS.
b) Broad signal with another coupling J=*ca.* 1 Hz.
c) Assignment may be reversed in each column.



12 **13** **10b** **14a** : R=H **14b** : R=Ac

Chart 3

hydrogenation of its acetate (**10b**) in EtOH or AcOH gave the *cis*-decalone (**14b**) (**14a**, mp 111°C; acetate **14b**, mp 111°C). Similarly, on hydrogenation with PtO_2, the alcohol (**10a**) gave a *trans*-decalol, whereas the acetate (**10b**) gave a *cis*-decalol. On the other hand, Narang and Dutta[8] obtained the *trans*-decalone (**11b**) (mp 113°C), though in low yield, by hydrogenation of the acetate (**10b**) in AcOH over PtO_2 (after re-oxidation). The stereochemistry of our decalone was definitively established as *trans* by X-ray crystallography of the derived *p*-bromobenzoates (**16c** and **18c**) (see below).

From **11a**, the 4,4-dimethyl-3-ketones were synthesized as follows. Reduction of **11a** with sodium and *n*-propanol yielded the thermodynamically more stable 8α-alcohol (**15a**) as a major product. In the ^{1}H-NMR spectrum the broad signal (Wh/2=19 Hz) at δ 3.81 geminal to the hydroxyl in addition to the 3α-proton (δ 3.25 ppm) indicated that the newly formed hydroxyl group is in an equatorial orientation. Partial acetylation of this product with Ac_2O–pyridine in the cold yielded the mono-acetate (**15b**), in which acetylation of the less hindered 8α-hydroxyl (the 3β-hydroxyl group is at a neo-pentyl position) was deduced from the ^{1}H-NMR spectrum: the signal at δ 3.81 ppm shifted to δ 4.95 ppm, while that at δ 3.25 ppm

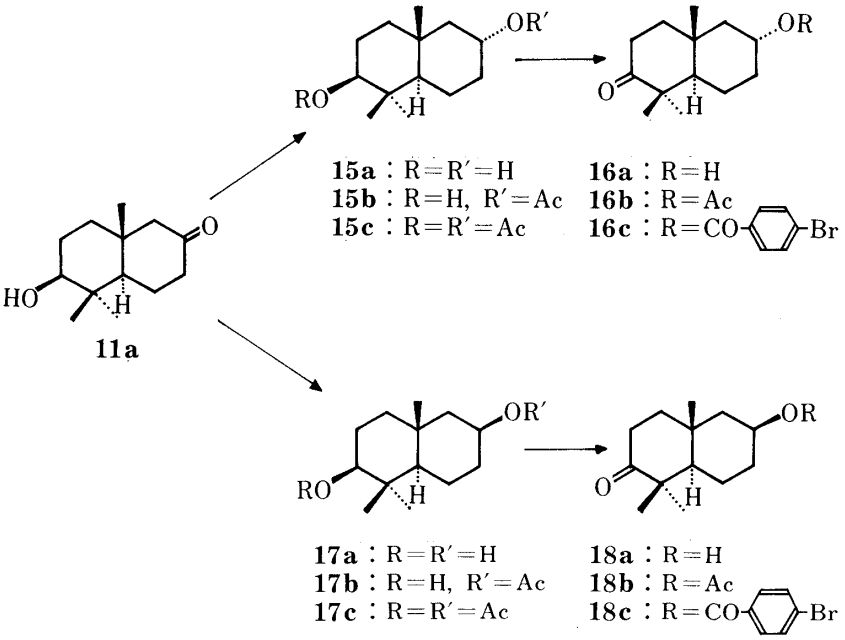
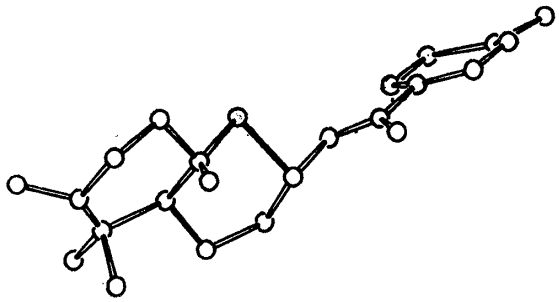


Chart 4

remained almost unchanged. Jones oxidation of **15b** gave the desired 8α-acetoxy-3-one (**16b**), which was hydrolyzed to the 8α-hydroxy derivative (**16a**). It formed a *p*-bromobenzoate (**16c**), mp 128°C.

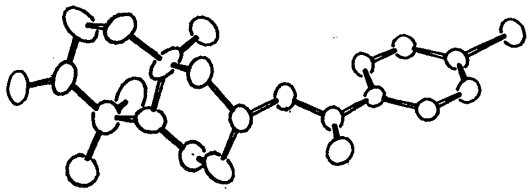
On the other hand, hydride reduction of **11a** was expected to yield the 8β-alcohol predominantly, since a hydride anion would approach from the less hindered α-face. In fact, **11a** was reduced by $LiAlH(OBu\text{-}t)_3$ in ether to yield a 3:1 mixture of 8β-alcohol (**17a**) and 8α-alcohol (**15a**), from which the 8β-alcohol (**17a**), mp 193—194°C, was separated in pure form by chromatography. It gave the diacetate (**17c**), mp 107°C. In the ^{1}H-NMR spectrum of **17c**, the multiplet signal of the 3α-proton at δ 4.51 ppm, and the appearance of a triplet (J = 2.8 Hz) at δ 5.08 ppm indicated that the C_8-acetoxyl group is in an axial orientation. Halsall *et al.*[7] obtained a single 3β,8ξ-decalol, mp 190°C, by hydrogenation of **11a** in AcOH over PtO_2. High stereoselectivity of this hydrogenation was confirmed and the product was proved to be identical with the 8β-alcohol (**17a**) by re-examination of their experiment. Partial hydrolysis of **17c** with K_2CO_3 in methanol resulted in hydrolysis of the equatorial 3β-acetoxy group giving rise to **17b** as a major product. Up-field shift of the multiplet signal at δ 4.51 to δ 3.24 ppm in the ^{1}H-NMR spectrum corroborated its structure. Jones oxidation of **17b** gave the 8β-acetoxy-3-one (**18b**), which was hydrolyzed to the 8β-hydroxy derivative (**18a**). It formed the *p*-bromobenzoate (**18c**), mp 133°C.

The two *p*-bromobenzoates, **16c** and **18c**, were subjected to single crystal X-ray analysis.[16] The crystal data are given in the legend to Fig. 1. The intensity data were collected on a Philips PW-1100 diffractometer using graphite-monochromated Cu–$K\alpha$ radiation, and 3036 and 2335 reflections having intensities above the $2\sigma(I)$ level were recorded for **16c** and **18c**, respectively. The structures were solved by the heavy atom method. Block-diagonal least-squares refinement with anisotropic temperature factors for all non-hydrogen atoms reduced the R factors to 0.17 and 0.115 for **16c** and **18c**, respectively. The resulting molecular structures are shown in Fig. 1; the results established that the compounds have *trans* configurations. Unfortunately, in the case of **16c** two independent molecules in an asymmetric unit formed a pseudo-symmetric pair and in the refinement when one molecule was converging, the other tended to diverge. The use of the full-matrix least-squares method and an extended computation time might have reduced R below 0.17.



16c

Crystal data: $C_{20}H_{25}BrO_3$,
MW=393.3, triclinic,
space group $P\bar{1}$,
$a=25.329$, $b=11.318$,
$c=7.107$Å, $\alpha=107.85$, $\beta=80.23$,
$\gamma=101.62°$, $Z=4$, $U=1886.8$Å^3,
$Dx=1.385$ g·cm^{-3}



18c

Crystal data: $C_{20}H_{25}BrO_3$,
MW=393.3, monoclinic,
space group $P2_1/c$
$a=7.432$, $b=39.449$,
$c=7.106$Å, $\beta=115.79°$,
$Z=4$, $U=1875.9$Å^3,
$Dx=1.393$ g·cm^{-3}

Fig. 1. Computer-generated Perspective Drawings of **16c** and **18c**

^{1}H- and ^{13}C-NMR Spectra and Conformational Analysis

X-Ray analyses of **16c** and **18c** showed that the 8α- and 8β-isomers both have distorted chair conformations at ring A. This is also true for a 4,4-dimethylsteroid 3-ketone.[17] Calculation[18] of the dihedral angles between the 4β-methyl group and the carbonyl plane suggested that the angle in the 8β-isomer (108°) is smaller than that in the 8α-isomer (116°). This implies that ring A of the 8β-isomer is more flattened, although this comparison is only a qualitative one, since the *R*-values were not sufficiently small for quantitative estimation (see above).

In order to determine the conformations in solution, the ^{13}C-NMR spectra of the stereoisomeric pairs were compared (Table II). The signal assignments are based on various off-resonance techniques, ^{1}H-selective hetero-spin decoupling with the use of known chemical shift rules (α-, β-, and γ-effect,[19] *syn*-diaxial effect[20,22] the acylation shift rule [21]), and comparison with literature data for 10β-methyl-*trans*-decalols[22] and triterpenoid 3-ketones.[23] Three methyl signals were differentiated by use of their TH effect (see below) together with ^{1}H-selective hetero-spin decoupling. To simplify discussion the differences of δ_C for each

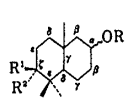
TABLE II. ^{13}C-Chemical Shifts of 4,4, 10β-Trimethyldecalins **15**, **16**, **17**, and **18** in $CDCl_3$ (ppm)

Carbon No.	15a	15b	15c	16a	16b	16c	17a[a]	17b	17c	17c[a]	18a	18b	18c
1	39.7	39.6	39.2	39.9	39.9	39.9	41.3	40.0	39.6	39.7	40.6	40.3	40.2
2	27.3	27.7	23.7	34.8	34.3	34.4	28.1	27.0	23.5	23.8	34.5	34.5	34.4
3	79.1	79.0	80.7	216.5	215.9	215.8	78.6	79.0	80.8	80.6	216.8	216.3	216.1
4	38.6	38.6	37.6	47.5	47.6	47.7	39.5	38.6	37.6	37.8	47.7	47.6	47.5
5	52.1	52.0	52.1	52.6	52.5	52.6	53.8	52.7	52.8	52.5	53.5	53.1	53.1
6	20.7	19.7	19.8	21.3	21.4	21.4	17.7	17.3	17.3	17.5	17.8	18.4	18.6
7	36.8	32.5	32.5	34.3	32.1	32.1	35.9	31.7	31.7	31.8	33.7	31.2	31.2
8	67.1	70.2	70.1	66.8	69.9	70.9	66.5	70.0	70.0	70.0	66.9	69.6	70.8
9	53.9	49.6	49.5	52.6	48.5	48.5	51.5	47.3	47.2	47.2	49.5	46.3	46.5
10	35.1	35.1	33.8	36.0	34.9	35.1	34.7	33.9	33.8	33.9	34.2	33.6	33.6
11	28.1	27.9	27.8	25.6	25.5	25.4	28.7	27.8	27.8	27.8	25.7	25.8	25.7
12	20.0	20.4	20.8	21.5	21.4	21.3	22.1	20.7	20.8	21.0	21.4	21.4	21.4
13	15.0	15.0	16.2	19.1	18.9	18.9	16.1	15.0	16.2	16.4	20.5	19.9	20.3

a) In pyridine-d_5.

TABLE III. Effect on δ_C caused by Orientational Difference of C_8-Substituent ($\Delta\delta=\delta_{ax}-\delta_{eq}$)

	Ring B						Ring A				Me		
	α	β		γ		δ	δ	ε		ζ	δ	ζ	
	C_8	C_7	C_9	C_6	C_{10}	C_5	C_1	C_2	C_4	C_3	C_{13}	C_{11}	C_{12}
17b—15b	−0.2	−0.8	−2.3	−2.5	−1.2	+0.7	+0.4	−0.2	0	+0.1	+0.1	−0.1	+0.4
17c—15c	−0.1	−0.8	−2.3	−2.4	−1.2	+0.7	+0.4	−0.2	0	0	0	−0.1	+0.3
18a—16a	+0.1	−0.6	−3.1	−3.5	−1.8	+0.9	+0.7	−0.3	+0.2	+0.3	+1.4	+0.1	+0.1
18b—16b	−0.3	−0.9	−2.0	−3.0	−1.3	+0.6	+0.4	+0.2	0	+0.4	+1.0	+0.3	0
18c—16c	−0.1	−0.9	−2.0	−2.8	−1.5	+0.5	+0.3	0	−0.2	+0.3	+1.4	+0.3	+0.1
Decalin **19**[a]	+0.7	−3.1	−2.3	−3.9	−1.2	+1.0	+0.3	0	+0.6	+0.1			
Steroid **20**[b]	+0.1	−2.9	−2.4	−3.8	−1.5	+1.0	+0.9	+0.1	+0.7	+0.1			



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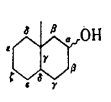

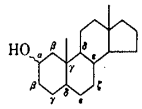

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a) S.H. Grover and J.B. Stothers, *Canad. J. Chem.*, **52**, 870 (1974).
b) H. Eggert, C.L. Van Antwerp, N. S. Bhacca, and C. Djerassi, *J. Org. Chem.*, **41**, 71 (1976).

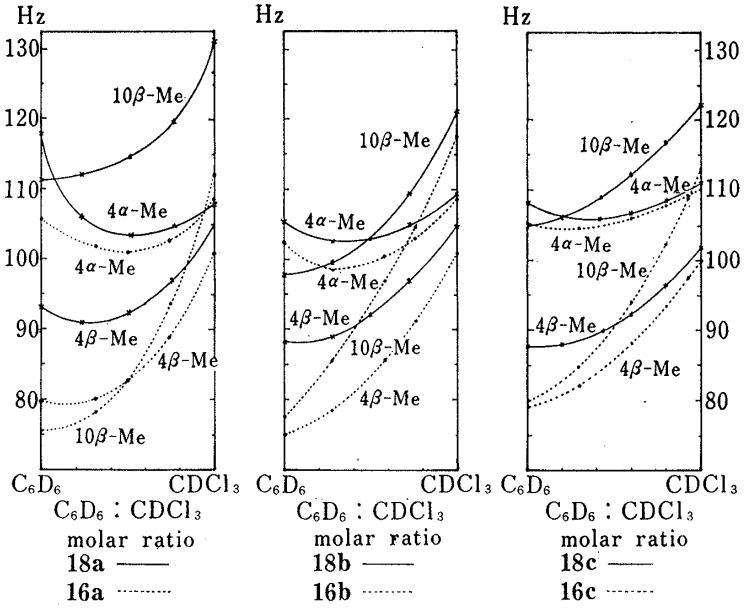
epimeric pair, $\Delta\delta=\delta(8\beta)-\delta(8\alpha)$ due to orientational difference of the C_8-substituent have been collected in Table III, together with the data for a 10β-methyl-*trans*-decalin[22] and a steroid,[24] which bear no 4,4-dimethyl group, for comparison.

Usually an axial hydroxyl group shields the α-carbon atom more than does an equatorial hydroxyl group. Grover and Stothers[22] showed that this rule is inapplicable where the hydroxyl group takes part in a *syn*-diaxial interaction which violates the general premise that associates steric crowding with up-field shifts for C_α, C_β, and C_γ.[19] In our compounds, all of the 8β-isomers have a *syn*-diaxial OR–Me interaction. In each of these, the α-effect is accentuated such that the axial hydroxyl (or acyloxyl) group deshields the carbinyl carbon more than does its equatorial counterpart. Thus $\Delta\delta_\alpha$(ax-eq) at C_α is −0.3—+0.1. For the two C_β positions, C_7 and C_9, both of which are methylene carbons, there were remarkable differences in $\Delta\delta_\beta$'s (−2.0——3.1 at C_7 and −0.6——0.9 at C_9), in distinct contrast to the cases of 10β-methyl-*trans*-decalols [22] and steroids[24] which bear no 4,4-dimethyl group and had comparable $\Delta\delta_\beta$'s for both C_β's (−2.0——3.0). The $\Delta\delta_\gamma$, at both C_6(methylene) and C_{10} (quat. carbon) showed the usual trend (−2.5——3.5 at C_6 and −1.2 ——1.8 at C_{10}). Differences of the δ-effect ($\Delta\delta_\delta$) on the 10β-methyl group were small (0—+0.1) in 3-hydroxy and 3-acetoxy derivatives, but were significant (+1.0—+1.4) in 3-keto derivatives. The value reported for decalins[22] and steroids[24] were close to the latter values.

Differences of shieldings on the second ring carbons, which may reflect the transmission of the steric compression due to the 8-axial sustituent, were too small and indefinite for evaluation.

^{1}H-NMR spectra of the 8α- and 8β-substituted-3-ones (**16** and **18**) again were not very informative as regards conformational differences at ring A: stereochemical changes at C_8 did not produce any significant difference in the chemical shift of either the 4α- or 4β-methyl group. However, the ASIS shift seen on continuously changing the solvent from chloroform-*d* to benzene-d_6 (TH effect)[25] showed a clear difference between the 8α- and 8β-isomer.

It is known[25,26] that for carbonyl compounds, on changing the solvent from $CDCl_3$ to benzene, the protons in front of the reference plane (the same side as the carbonyl oxygen) which is at right angles to the carbonyl plane and cuts through the carbonyl carbon rectangularly to the C–O bond, shift down-field ($H=\delta_{CDCl_3}-\delta_{benzene}<0$), while the protons rear the reference plane shift up-field ($H>0$). The protons near or on that plane show a negli-



Figs. 2-4, TH Effect of C-Methyls of 8α and 8β-Substituted-4,4,10β-trimethyl-*trans*-decal-3-ones (100 MHz)

gible shift (H—0) but have rather large T(T=deviation from the straight line). In fact, 4α- and 4β-methyl in **16b** experience markedly different TH effects, indicating that 4α-methyl protons are nearer to the reference plane than 4β-methyl protons ($H_{4\beta\text{-Me}}=+26$[27], $H_{4\alpha\text{-Me}}=+7$) as expected from the chair-like conformation of ring A. Comparison of the TH curves of the epimeric pairs, **16** and **18**, immediately confirmed the assignments of the methyl signals and also indicated that ring A of the 8β-isomer is more flattened than that of the corresponding 8α-isomer. The shapes of the TH curves of 4α- and 4β-methyl became closer in the 8β-isomers, showing that relationship of both methyls to the reference plane is becoming similar (*e.g.* for **18b**, $H_{4\beta\text{-Me}}=+16$, $H_{4\alpha\text{-Me}}=+3$). Chair-like conformation of ring A in this compound (**18a**) was also supported by the TH curve of the 10β-methyl protons. Usually an axial methyl at the γ-position to the carbonyl group in a cyclohexanone ring shows a large up-field shift ($H\gg0$) when the ring has the chair conformation (*e.g.* 10β-methyl of steroid 3-ketone), while it shows negative or negligible shift ($H\lesssim0$) with rather large T when the ring has the boat conformation (*e.g.* 18α-methyl of 14β-serratan-15-one) since its protons fall in the negihborhood of the reference plane.[25] On the other hand, a methyl of eclipsed or parallel orientation with a hydroxyl group shows negligible H (+2——2) with considerably larger T (4—5).[25] As expected, the 10β-methyl of the 8α-isomer (**16a**) exhibited large positive H (+36), but that of the 8β-isomer (**18a**) showed smaller H (+20). The latter curve is best explained as a combination of the effects of 3-one and 8β-OH. If the compound had boat conformation at ring A, the 10β-methyl would show negligible or negative H with rather large T.

Thus, the conclusions obtained in solution agree qualitatively with the results of X-ray analyses: the 8α- and 8β-isomers have distorted chair conformations at ring A, which is more flattened in 8β-isomers, apparently due to the transmission of steric compression.

Another conclusion of the present investigation is that, among the various spectroscopic methods (except for CD of optically active compounds), measurement of the TH effect best reflects small changes in the conformation of ring A induced by a stereochemical change at another part of the molecule.

Experimental

Unless otherwise stated, melting points were determined on a Yanagimoto micro hot-stage mp apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Jasco IR-G spectrometer as KBr discs and

are given in cm^{-1}. ^1H-NMR spectra were taken in $CDCl_3$ solution (with TMS as an internal standard) on a JEOL JNMPS-100 (100 MHz) or JNM PMX-60 (60 MHz) spectrometer. Chemical shifts are given on the δ (ppm) scale: s, singlet; d, doublet; t, triplet; m, multiplet. Kieselgel GF_{254} nach Stahl, type 60, and Wakogel C-200 (Silica gel) were used for TLC and column chromatography, respectively. All organic extracts were washed with water and dried over Na_2SO_4 before concentration. Identities were confirmed by thin-layer chromatography (TLC), IR, and NMR comparisons.

2-Ethoxycarbonyl-4,4-ethylenedioxycyclohexanone (3)——Diethyl γ,γ-ethylenedioxypimelate[8] (30 g) and NaH (60% oil-coated NaH, 12 g, was washed with *n*-hexane) in ether (300 ml) were heated together under reflux with stirring for 7 h in an argon atmosphere. The cooled mixture was quenched with AcOH, poured into ice-water, and extracted several times with ether. The combined ethereal layer was washed with saturated aqueous $NaHCO_3$ solution, water, dried, and concentrated. Crystallization of the residue from *n*-hexane gave **3** (22 g, 87%), as colorless prisms, mp 47—48°C. IR: 1645, 1605. NMR: δ 1.27 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 3.92 (4H, s, $-OCH_2CH_2O-$), 4.15 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$). *Anal.* Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 57.90; H, 7.35.

10-Ethoxycarbonyl-6,6-ethylenedioxy-$\Delta^{1(9)}$-octal-2-one (4)——A mixture of cyclohexanone **3** (20 g), methyl vinyl ketone (14 g), and triethylamine (4.4 ml) in MeOH (220 ml) was stirred for 40 h at room temp. in an argon atmosphere. The solvent was evaporated off *in vacuo* and the residue was dissolved in benzene. The solution was washed with 2% HCl, water, dried, and concentrated to give an adduct as a gum. This was dissolved in benzene, then pyrrolidine (1.45 ml) and AcOH (1.06 g) were added at 0°C, and the mixture was heated under reflux for 1 h using a Dean-Stark water separator. When no further water could be removed, the solvent was evaporated off *in vacuo* and the residue was dissolved in ether. The solution was washed with 2% HCl, water, dried, and concentrated. Crystallization of the residue from *n*-hexane–ether gave the enone **4** (12.6 g, 53%), as colorless prisms, mp 71—74°C. IR: 1720, 1668. NMR: δ 1.26 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 3.89 (4H, s, $-OCH_2CH_2O-$), 4.09 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.89 (1H, bs, H-1). *Anal.* Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.10; H, 7.17.

10-Ethoxycarbonyl-6,6-ethylenedioxy-1,1-dimethyl-Δ^{8}-octal-2-one (5)——The enone **4** (10 g) in *t*-BuOH (60 ml) was stirred with a solution of *t*-BuOK in *t*-BuOH prepared from 100 ml of *t*-BuOH and 3.2 g of K. CH_3I (30 ml) was added to the resulting brown mixture all at once and the resulting milky mixture was heated under reflux for 40 min. After cooling, the mixture was poured into water, and extracted with $CHCl_3$. The organic layer was washed with water, dried, and concentrated to yield a gum which, on crystallization from *n*-hexane–ether, gave **5** (9 g, 82.7%) as colorless prisms, mp 93—94°C. IR: 1704. NMR: δ 1.20 (3H, t, J=7.5 Hz, $COOCH_2C\underline{H}_3$), 1.28, 1.40 (each 3H, s, CH_3), 3.89 (4H, $-OCH_2CH_2O-$), 4.03 (2H, q, J=7.5 Hz, $COOC\underline{H}_2CH_3$), 5.66 (1H, t, J=4 Hz, H-8). *Anal.* Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.32; H, 7.96.

The Lactone (6)——i) The dimethyl derivative **5** (4.2 g) and $NaBH_4$ (750 mg) in MeOH (60 ml) were heated under reflux for 1 h. After addition of water, the mixture was extracted with CH_2Cl_2. The extract was dried and concentrated, and chromatography of the residue with benzene–AcOEt (6: 1) gave the lactone **6** (3.2 g, 88.6%), which crystallized as colorless prisms from *n*-hexane–ether, mp 93—95°C. IR: 1740. NMR: δ 1.17 (6H, s, $CH_3\times2$), 3.92 (4H, $-OCH_2CH_2O-$), 4.17 (1H, t-like, J=2 Hz, H-3), 5.47 (1H, t, J= 4 Hz, $-CH=$). *Anal.* Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.05; H, 7.63.

ii) The dimethyl derivative **5** (2 g) in EtOH (20 ml) containing EtONa (10 drops of 7% ethanolic solution) was hydrogenated over PtO_2 (1 g) for 15 h. Removal of the solvent and catalyst from the mixture, and crystallization of the residue as above gave the lactone **6** (1.5 g, 87.5%).

The Lactol (7)——The lactone **6** (1.5 g) and $LiAlH(OBu\text{-}t)_3$ (3 g) in ether (40 ml) were heated under reflux for 9 h. After the decomposition of excess reagent with water, the ethereal layer was separated by decantation, and the residue was extracted with CH_2Cl_2. The combined organic layer was dried and concentrated to give a solid which was purified by chromatography. Elution of the column with benzene–AcOEt (6: 1) gave the lactol **7** (1.1 g, 78.8%), which crystallized from *n*-hexane–ether as colorless prisms, mp 99—101°C. IR: 3350. NMR: see Table I. *Anal.* Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.19; H, 8.11.

The crystalline lactol **7a** was acetylated with an excess of Ac_2O and pyridine (1: 2). The product, on work-up as usual, gave the acetate **8a**, as colorless needles from *n*-hexane, mp 103—105°C. IR: 1730. NMR: see Table I. *Anal.* Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.39; H, 7.98.

6,6-Ethylenedioxy-1,1,10β-trimethyl-Δ^{8}-octalin-2β-ol (9)——The lactol **7** (1 g) and anhyd. hydrazine (0.4 ml) were heated in diethyleneglycol (15 ml) containing Na (300 mg) at 150—170°C for 2.5 h in an argon atmosphere. The temperature was raised to 210°C to remove excess hydrazine, then the mixture was maintained at 230—240°C (bath temp.) for a further 1.5 h. Water was added to the cooled mixture, which was extracted with CH_2Cl_2. Removal of the solvent from the extract and chromatography of the residue gave the trimethyl derivative **9** (617 mg, 65%) as an oil (lit.[8] oil). IR (neat): 3430. NMR: δ 1.07, 1.17, 1.30 (each 3H, s, CH_3), 3.92 (4H, s, $-OCH_2CH_2O-$), 5.46 (1H, t, J=3 Hz, H-8).

6β-Hydroxy-5,5,9β-trimethyl-*trans*-decal-2-one (**3β-Hydroxy-4,4,10β-trimethyl-*trans*-decal-8-one**) (11a)——The trimethyl derivative **9** (600 mg) in 60% AcOH (15 ml) was heated under reflux for 1 h in an argon atmosphere. After cooling, the mixture was diluted with EtOH (20 ml) and hydrogenated over 10% Pd-C (1 g) for 4 h. Removal of the solvent and catalyst from the mixture left a gum which was purified in CH_2Cl_2

by passage through a short column of Silica gel. Crystallization of the product from *n*-hexane–ether yielded the *trans*-decalone **11a** (263 mg, 52.8%) as colorless prisms, mp 116—118°C (lit. 144—145°C, sublim. at 115°C).[7] IR: 3400, 1690. NMR: δ 0.73, 0.89, 1.07 (each 3H, s, CH_3), 3.30 (1H, m, $Wh/2=15$ Hz, H-6). *Anal.* Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 73.99; H, 10.56.

On acetylation with Ac_2O and pyridine it formed the acetate **11b**, colorless prisms from *n*-hexane, mp 110—112°C (lit. mp 113°C).[7,8] IR: 1715, 1693. NMR: δ 0.92 (6H, s, $CH_3\times2$), 0.95 (3H, s, CH_3), 2.07 (3H, s, OAc), 4.60 (1H, m, H-6).

1,1,10β-Trimethyl-*trans*-decal-2β,6α-diol (4,4,10β-Trimethyl-*trans*-decal-3β,8α-diol) (15a)——Na (250 mg) was added portionwise to a stirred solution of the *trans*-decalone **11a** (200 mg) in *n*-propanol (3 ml) during 30 min, and the mixture was heated at 80°C for 30 min. The cooled mixture was poured into water and extracted with CH_2Cl_2. The product obtained from the extract was chromatographed on a Silica gel column in benzene. Elution was carried out successively with benzene, benzene–AcOEt, and AcOEt. The benzene and benzene–AcOEt eluates gave the starting material **11a** (70 mg) and the AcOEt eluate gave the 2β,6α-diol **15a** (102 mg), colorless prisms from ether, mp 139—140°C (partially sublimed). IR: 3300. NMR: δ 0.75, 0.94, 0.99 (each 3H, s, CH_3), 3.24 (1H, m, H-2), 3.81 (1H, m, H-6). *Anal.* Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.41; H, 11.28.

On acetylation overnight with an excess of Ac_2O–pyridine, **15a** gave the diacetate **15c**, as a colorless gum. IR (neat): 1740, 1728. NMR: δ 0.84, 0.88, 1.01 (each 3H, s, CH_3), 2.01, 2.05 (each 3H, s, Ac), 4.50 (1H, m, H-2), 4.91 (1H, m, H-6).

Partial Acetylation of the 2β,6α-Diol (15)——The 2β,6α-diol **15a** (90 mg) was stirred with Ac_2O (1 ml) and pyridine (5 ml) for 1.5 h at room temperature. The reaction mixture was poured into ice-water and extracted with CH_2Cl_2. The extract was washed with water, dried, and concentrated. Chromatography of the residue with benzene gave the diacetate **15c** (20 mg). Subsequent elution with benzene–AcOEt (15: 1) gave the 6α-monoacetate **15b** (55 mg), colorless prisms from *n*-hexane, mp 86—88°C. IR: 3400, 1728. NMR: δ 0.76, 0.88, 0.99 (each 3H, s, CH_3), 2.00 (3H, s, Ac), 3.24 (1H, m, H-2), 4.94 (1H, m, H-6). *Anal.* Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 71.02; 10.43.

1,1,10β-Trimethyl-*trans*-decal-2β,6β-diol (4,4,10β-Trimethyl-*trans*-decal-3β,8β-diol) (17a)——i) The *trans*-decalone **11a** (200 mg), and $LiAlH(OBu\text{-}t)_3$ (1 g) in ether (30 ml) were heated under reflux for 3 h. After decomposition of the excess reagent with water, the ethereal layer was separated, and the residue was extracted with ether. The combined ethereal layer was washed with water, dried, and concentrated to leave a gum, which was chromatographed in benzene. Elution with benzene–AcOEt (10: 1) gave the 2β,6β-diol **17a** (151 mg, 75%), mp 193—194°C. IR: 3300. NMR (C_5D_5N): δ 1.11, 1.26, 1.49 (each 3H, s, CH_3), 3.50 (1H, m, H-2), 4.32 (1H, t-like, $J=2.8$ Hz, H-6). *Anal.* Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.48; H, 11.30. The subsequent eluate with benzene–AcOEt (2: 1) gave the 2β,6α-diol **15a**, (50 mg, 25%), mp 139—140°C.

ii) The *trans*-decalone **11a** (50 mg) in AcOH (5 ml) was hydrogenated over PtO_2 (50 mg) for 8 h as described by Halsall *et al.*[7] Removal of the solvent and catalyst from the mixture gave the diol **17a** (50 mg) colorless prisms from *n*-hexane–ether, mp 193—194°C (lit.[7] mp 190°C); this product was identical with the 2β,6β-diol **17a** described above.

On acetylation with excess Ac_2O-pyridine, **17a** gave the diacetate **17c**, colorless needles from *n*-hexane–ether, mp 107°C. IR: 1723 (br). NMR: δ 0.88 (6H, s, $CH_3\times2$), 1.07 (3H, s, CH_3), 2.03, 2.05 (each 3H, s, Ac), 4.51 (1H, m, H-2), 5.02 (1H, t-like, $J=2.8$ Hz, H-6). *Anal.* Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.75; H, 9.53.

Partial Hydrolysis of the 2β,6β-Diacetate (17c)——The 2β,6β-diacetate **17c** (120 mg) in 5% K_2CO_3–MeOH (6 ml) was heated under reflux for 2 h. The mixture was poured into ice-water, extracted with CH_2Cl_2, and the product obtained from the extract was chromatographed in benzene. The benzene eluate gave the starting material **17c** (20 mg), and the benzene–AcOEt (20: 1) eluate gave the 6β-monoacetate **17b** (75 mg), colorless needles from *n*-hexane, mp 93—94°C. IR: 3300, 1728. NMR: δ 0.80, 1.00, 1.03 (each 3H, s, CH_3), 2.03 (3H, s, Ac), 3.21 (1H, m, H-2), 5.01 (1H, t-like, $J=2.8$ Hz, H-6). *Anal.* Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.52; H, 10.19.

The AcOEt eluate gave the diol **17a** (14 mg).

6α-Acetoxy-1,1,10β-trimethyl-*trans*-decal-2-one (8α-Acetoxy-4,4,10β-trimethyl-*trans*-decal-3-one) (16b)——Jones reagent (5 drops) was added to a stirred solution of **15b** (50 mg) in acetone (6 ml) at 0°C and stirring was continued for 20 min. The mixture was poured into water and extracted with ether. Removal of the solvent from the dried extract and crystallization of the residue from *n*-hexane gave 6α-acetoxy-2-one **16b** (40 mg), as colorless needles, mp 95—97°C. IR: 1728, 1704. NMR: δ 1.01, 1.09, 1.18 (each 3H, s, CH_3), 2.02 (3H, s, Ac), 4.94 (1H, m, H-6). *Anal.* Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.32; H, 9.61.

6β-Acetoxy-1,1,10β-trimethyl-*trans*-decal-2-one (8β-Acetoxy-4,4,10β-trimethyl-*trans*-decal-3-one) (18b)——The 6β-monoacetate **17b** (60 mg) was similarly oxidized and worked up as above to give 6β-acetoxy-2-one **18b** (52 mg) as a gum. IR: 1735, 1708. NMR: δ 1.05, 1.10, 1.22 (each 3H, s, CH_3), 2.06 (3H, s, Ac), 5.06 (1H, t-like, $J=2.8$ Hz, H-6).

6α-Hydroxy-1,1,10β-trimethyl-*trans*-decal-2-one (8α-Hydroxy-4,4,10β-trimethyl-*trans*-decal-3-one) (16a)——The 6α-acetate **16b** (50 mg) was hydrolyzed with 5% KOH–MeOH (4 ml) for 3 h at 80°C. The mixture

was poured into water and extracted with CH_2Cl_2. The extract was washed with water and concentrated to give the 6α-ol **16a** (46 mg) as a gum. IR (neat): 3350, 1685. NMR: δ 1.00, 1.09, 1.12 (each 3H, s, CH_3), 3.88 (1H, m, H-6).

6β-Hydroxy-1,1,10β-trimethyl-*trans*-decal-2-one (8β-Hydroxy-4,4,10β-trimethyl-*trans*-decal-3-one) (18a)——The 6β-monoacetate **18b** (36 mg) was hydrolyzed and worked up as above to yield the 6β-ol **18a** (30 mg), as colorless prisms from *n*-hexane, mp 93—94°C. IR: 3450, 1682. NMR: δ 1.06, 1.09, 1.32 (each 3H, s, CH_3), 4.15 (1H, t-like, J=2.8 Hz, H-6). *Anal.* Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.12; H, 10.56.

6α-*p*-Bromobenzoyloxy-1,1,10β-trimethyl-*trans*-decal-2-one (8α-*p*-Bromobenzoyloxy-4,4,10β-trimethyl-*trans*-decal-3-one) (16c)——The 6α-ol **16a** (20 mg) and *p*-bromobenzoyl chloride (40 mg) in pyridine (1.5 ml) were heated at 50—60°C for 1.5 h. After cooling, the mixture was poured into water and extracted with CH_2Cl_2. The extract was washed with 5% Na_2CO_3 and water, dried, and concentrated. Chromatography of the residue with benzene gave 6α-*p*-bromobenzoate **16c** (24 mg), colorless prisms from MeOH, mp 133°C. IR: 1701, 1582. NMR: δ 1.04, 1.12, 1.25 (each 3H, s, CH_3), 5.12 (1H, m, H-6), 7.31, 7.82 (each 2H, d, J= 8.6 Hz, Ar–H).

6β-*p*-Bromobenzoyloxy-1,1,10β-trimethyl-*trans*-decal-2-one (8β-*p*-Bromobenzoyloxy-4,4,10β-trimethyl-*trans*-decal-3-one) (18c)——*p*-Bromobenzoylation of the 6β-ol **18a** (30 mg) as described above gave the 6β-*p*-bromobenzoate **18c** (47 mg), colorless prisms from *n*-hexane, mp 128°C. IR: 1705, 1585. NMR: δ 1.07, 1.12, 1.29 (each 3H, s, CH_3), 5.27 (1H, t-like, J=2.8 Hz, H-6), 7.60, 7.91 (each 2H, d, J=8.6 Hz, Ar–H).

Acknowledgement The authors wish to thank Mr. Y. Itatani and Misses Y. Arano and J. Yasui of this Faculty for NMR measurement, elementary analyses and technical assistance. Thanks are also due for financial support for a part of this work by a Grant-in-Aid (No. 457520) for Scientific Research from the Ministry of Education, Science and Culture, Japan.

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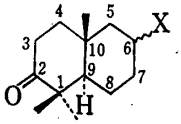

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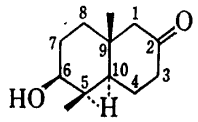

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27) We wish to propose the following notations for estimation of the magnitudes of H and T, which are independent of the magnetic fields.

$$H = (\text{shift})\text{ppm} \times 10^2$$
$$T = (\text{deviation})\text{ppm} \times 10^2$$

The previously reported values[25] in Hz must be variable, depending on the magnetic field used. Such values (H' or T') at 60 MHz are transformable to H and T by the following equation.

$$H \text{ or } T = 10/6 \times (H' \text{ or } T')$$