Note

Conformation of Pinan-3-ol Derivatives*

Chikao NISHINO and Hisao TAKAYANAGI

Mitsubishi-Kasei Institute of Life Sciences,
11 Minamiooya, Machida-shi, Tokyo 194, Japan

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In connection with our investigations on the structure-activity relationships of the sex pheromone mimic, (+)-*trans*-verbenyl acetate, of the American cockroach (*Periplaneta americana* L.), we synthesized 2,6,6-trimethylbicyclo[3.1.1]heptan-3-ol (pinan-3-ol) derivatives (1~6) according to the known (see references in the Figure) and usual synthetic procedures, and carried out configurational and conformational analyses of the

alcohols using the PMR spectra with the shift reagent, $\text{Eu}(\text{dpm})_3$, by the methods for the C-2 hydroxyl isomers.^{1,2)}

In each reaction product, an impurity or significant mixture [4 in 3 (2:7) and myrtenol* in 5 (1:2)] was separated from the major product by silicic acid chromatography. The physical data of the alcohols, whose purity was established to be almost 100% ($\geq 98\%$) by GC analysis (3% OV-225, 110°C), will be described later.

The mixture of the alcohol and $\text{Eu}(\text{dpm})_3$ (1:0.4, relative ratio)¹⁾ was subjected to PMR measurement (in CDCl_3 at 100 MHz) for the configurational analysis. The results are summarized in Table I. In the magnitudes of the induced shift values of the C-9 and secondary methyls, and the H(α)-7 signals, we could see similar trends to those in the experiment with the C-2 alcohols,¹⁾ as follows.

On comparison of the C-8 and C-9 methyl signals, the induced shift values of the C-9 methyl signals (A in Table I) showed outstanding differences between *cis*-

a) Lithium diisopropylamide, b) Diethyl azodicarboxylate

FIGURE. Synthetic routes to alcohols 1~6 and their conformations.

* Studies on the Sex Pheromone Mimic of the American Cockroach, (+)-*trans*-Verbenyl Acetate. Part III. For Part II, see *Agric. Biol. Chem.*, 43, 2323 (1979).

* A hydroxyl migrated isomer of *trans*-pinocarveol (6) in the benzoxylation process.

TABLE I. CHEMICAL SHIFTS (ppm) OF 8-CH₃, 9-CH₃, 7-H(α) AND SECONDARY CH₃ OF PARIS OF *cis-trans* ISOMERS AND INDUCED SHIFTS (Δ ppm) OF THE PROTONS ON ADDITION OF Eu(dpm)₃ (0.08 m Mol) TO CDCl₃ (0.3 ml) SOLUTIONS OF THE SUBSTRATES (0.2 m Mol) IN THE PMR SPECTRA (100 MHz)

Compound	9-CH ₃	Δ ppm(A)	8-CH ₃	Δ ppm(B)	7-H(α) ^a	Δ ppm	sec-CH ₃ ^b	Δ ppm
(+)-Neoisopinocampheol (1)	1.07	2.81	1.19	1.07	1.05	1.92	1.09	3.96
(-)-Isopinocampheol (2)	0.92	1.34	1.23	0.90	1.05	3.15	1.13	2.21
(+)-Pinocampheol (3)	0.88	2.62	1.19	1.13	1.24	2.26	1.01	2.94
(-)-Neopinocampheol (4)	0.80	1.47	1.23	1.09	1.58	5.40	0.98	4.26
(+)- <i>cis</i> -Pinocarveol (5)	0.76	2.87	1.28	1.16	1.47	1.94	—	—
(-)- <i>trans</i> -Pinocarveol (6)	0.65	1.48	1.28	1.06	1.70	5.30	—	—

^a In all compounds, this proton appeared as a sharp doublet signal with $J=8.5\sim 10.0$.

^b This methyl signal showed a doublet with $J=6.0\sim 7.0$.

TABLE II. CHEMICAL SHIFTS AND SPLITTING PATTERNS OF DIFFERENT PROTONS AFTER ADDITION OF Eu(dpm)₃ (IN CDCl₃, 80 MHz)

Compound	Relative ratio alcohol/Eu(dpm) ₈	Protons, chemical shifts (ppm) and splitting patterns ^a								
1	1/0.3	3H	4H _(β) [3H,5H,7H _(β)] ^b		4H _(α) (3H,5H)	2H	1H,5H ^c	7H _(β)	7H _(α)	
		10.78	6.54		5.20	5.13	3.15	2.49	2.45	
		dt	tq		dq	m		m	d	
2	1/0.35	3H	2H		4H _(α) (3H)	4H _(β) [3H,5H,7H _(β)] ^d		7H _(α)	7H _(β)	1H,5H
		12.50	8.38		8.10	5.96		4.55	3.98	3.75
		m	m		dq	tq		d	m	
3	1/0.25	3H	2H(3H)		4H _(β) [3H,5H,7H _(β)]	4H _(α) (3H)		1H,5H,7H _(α) ,7H _(β)		
		9.60	6.06		5.80	4.90		near 2.20		
		dq	dt		bq	dq				
4	1/0.75	3H	4H _(α) (5H)		7H _(α)	2H	4H _(β) [5H,7H _(β)]		5H	1H,7H _(β)
		19.68	13.29		10.75	7.80	7.59		5.68	5.30
		m	q		d	m	tq		m	
5	1/0.4	3H	4H _(β) [5H,7H _(β)]		4H _(α) (5H)	1H	5H,7H _(β)		7H _(α)	
		13.20	8.10		6.46	4.42	3.63	3.41		
		m	bq		dq	t	d			
6	1/0.6	3H	4H _(α)		7H _(α)	4H _(β) [5H,7H _(β)]		1H	5H	7H _(β)
		14.89	10.31		8.38	6.03		5.23	4.95	4.35
		d	q		d	tq		t	tt	m

^a bq=broad quartet, d=doublet, dq=double quartet, dt=double triplet, m=multiplet, q=quartet, t=triplet, tq=triple quartet, tt=triple triplet.

^b Proton signals in parenthesis were irradiated.

^c Center of the unresolved multiplet signal.

^d This proton sometimes showed a tq pattern (1, 2, 4 and 6) made up of $J_{3,4\beta}$, $J_{4\beta,4\beta}$, and $J_{4\beta,5}=J_{4\beta,7\beta}=1.5\sim 2.5$ Hz.⁹⁾

and *trans*-alcohols, i.e., the A values in the *cis*-alcohols always were larger than those in the *trans*-alcohols. On the other hand, with the induced shift values of H(α)-7, much larger values were indicated in the *trans*-alcohols than in the *cis*-alcohols. For the secondary methyl proton signals, the methyl group having the same configuration as the hydroxyl group (β - β in 1 and α - α in 4) exhibited a larger down-field shift, compared with the methyl group with opposite relationships

(β - α in 2 and α - β in 3) as pointed out in the previous paper.¹⁾ Thus, the induced shift values of the signals of the methyls and H(α)-7 were shown to be also useful for determining the configuration of the C-2 methyl and C-3 hydroxyl groups in pinan-3-ol derivatives, when their PMR spectra were taken in the presence of a shift reagent.

For the conformational analysis, the PMR spectra of the alcohols were recorded at 80 MHz after addition

TABLE III. COUPLING CONSTANTS (J) BETWEEN PROTONS OF ALCOHOLS

Compound	$J_{1,2\alpha}$	$J_{1,2\beta}$	$J_{2\alpha,3\alpha}$	$J_{2\alpha,3\beta}$	$J_{2\beta,3\alpha}$	$J_{2\beta,3\beta}$	$J_{3\alpha,4\alpha}$	$J_{3\alpha,4\beta}$	$J_{3\beta,4\alpha}$	$J_{3\beta,4\beta}$	$J_{4\alpha,5}$	$J_{4\beta,5}$	
1	? ^a	—	9.6	—	—	—	9.6	5.3	—	—	14.3	4.0	1.5
2	?	—	—	5.0	—	—	—	—	4.4	8.8	14.3	1.9	2.4
3	—	?	—	—	6.6	—	9.5	7.9	—	—	13.4	4.1	?
4	—	?	—	—	—	?	—	—	0	8.0	15.2	3.9	2.0
5	—	—	—	—	—	—	9.7	7.4	—	—	13.5	3.9	?
6	—	—	—	—	—	—	—	—	0	7.7	15.1	3.8	1.8

^a The J value was impossible to read from the spectrum.

of an appropriate quantity of $\text{Eu}(\text{dpm})_3$. The chemical shifts and splitting patterns of different protons mutually separated in such spectra are listed in Table II. The read coupling constants are shown in Table III. Conformational figures in the Figure were obtained from the coupling constants through the Tori equation⁸⁾ and inspection of the Dreiding models.

Abraham *et al.*⁹⁾ were able to read coupling constants between vicinal protons of the pinicarveols (**5** and **6**) by the use of 220 and 300 MHz PMR apparatuses. Our coupling constants for the protons of **5** and **6** agreed with Abraham's data.⁹⁾ Consequently, the conformations of **5** and **6** were half bridged chair forms* as described by them.⁹⁾ Our coupling constant values for **1**~**4** showed good coincidences with the values reported by Jefford *et al.*,¹⁰⁾ so that the conformations of **1**~**4** are similar between Jefford's and our results, in which compounds **1**, **3** and **4** take half bridged chair forms, whereas compound **2** is a rather bridged boat form.* In the conformations of **2**~**4**, the stereointeraction of the C-9 methyl is maximally relieved from the group at quatorial methyl at the C-2 and the hydroxyl quasiethe C-3.

For the conformation of **1**, Jefford¹⁰⁾ and we similarly proposed a flattened bridged chair form, while Abraham *et al.*⁹⁾ disagreed with our opinion suggesting a flattened boat form. This conformational discrepancy may arise from the difference of the equations employed for the calculation from coupling constant to dihedral angle. This would severely affect the conformation close to the Y-shape,* especially.

If a typical bridged chair or boat form is taken for the conformation of **1**, the quasiaxial C-2 methyl or the similarly oriented hydroxyl may cause an undesirable interaction around the C-9 methyl. However, the interaction between the C-9 and C-2 methyls in our flattened chair form shows an almost equivalent congestion as compared with the interaction between the C-9 methyl and C-3 hydroxyl in the flattened boat form. Hence, the conformation of **1** is a question that requires further investigations.

PHYSICAL DATA OF THE ALCOHOLS¹¹⁾

(+)-*Neoisopinocampheol* (**1**): mp 37.5~41° (hexane); $[\alpha]_D + 34.7^\circ$ ($c=0.46$); IR (KBr): 3360 cm^{-1} ; MS: 136 ($M^+ - 18$), 70 (Base peak). (—)-*Isopinocampheol* (**2**): mp 51~52° (hexane); $[\alpha]_D - 35.4^\circ$ ($c=0.48$); IR (nujol): 3320 cm^{-1} ; MS: m/e 136 ($M^+ - 18$), 70 (Base peak). (+)-*Pinocampheol* (**3**): mp 61~63° (hexane); $[\alpha]_D + 59.7^\circ$ ($c=0.48$); IR (KBr): 3280 cm^{-1} ; MS: m/e 154 (M^+ , $\text{C}_{10}\text{H}_{18}\text{O}$), 139, 84 (Base peak), 70 (85%). (—)-*Neopinocampheol* (**4**): $[\alpha]_D - 15.1^\circ$ ($c=0.56$); IR (film): 3400 cm^{-1} ; MS: m/e 154 (M^+ , $\text{C}_{10}\text{H}_{18}\text{O}$), 139, 84 (Base peak), 70 (98%). (+)-*cis-Pinocarveol* (**5**): mp 40.5~42.5° (hexane); $[\alpha]_D + 45.5^\circ$ ($c=0.48$); IR (nujol): 3320, 1640, 890 cm^{-1} ; MS: m/e 152 (M^+ , $\text{C}_{10}\text{H}_{16}\text{O}$), 134, 92 (Base peak). (—)-*trans-Pinocarveol* (**6**): $[\alpha]_D - 54.9^\circ$ ($c=0.99$); IR (film): 3380, 1640, 890 cm^{-1} ; MS: m/e 152 (M^+ , $\text{C}_{10}\text{H}_{16}\text{O}$), 134, 92 (Base peak).

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* See ref. 2.

- 11) Specific rotations were measured in benzene at 25°. IR, PMR and MS spectra were taken with a JASCO IRA-1, a JEOL PS-100 (100 MHz) and Varian FT-80A system (80 MHz), and a Shimadzu GCMS-7000, respectively.
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