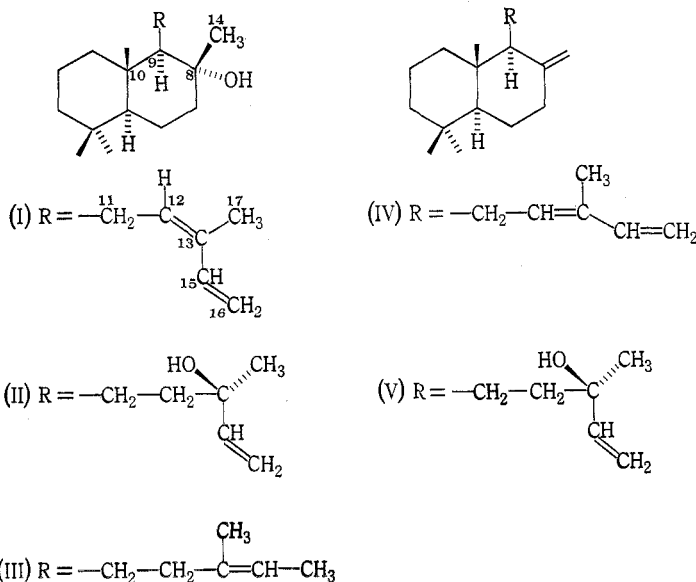


THE STEREOCHEMISTRY AND ABSOLUTE CONFIGURATION OF ABIENOL*

By R. M. CARMAN†

Abienol, the diterpenoid alcohol present in *Abies oleoresin*¹⁻⁵ and in particular obtainable from the oleoresin of *Abies balsamea* (Canada balsam),⁵ has been assigned³⁻⁵ the structure (I) (without stereochemical implications).



During a recent survey of optical rotation and structure in the bicyclic diterpenoid series,⁶ it was observed that abienol had an unexpectedly high rotation. If simple molecular rotation differences are meaningful, then abienol (I) should have a rotation approximately equal to that of sclareol (II) ($[M]_D -15$) plus biformene (IV) ($[M]_D +33$) minus manool (V) ($[M]_D +96$); i.e. a molecular rotation of -78 units. Abienol in fact⁵ has $[M]_D +70$ which led to the suggestion⁶ that abienol

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¹ Wienhaus, H., and Mucke, K., *Chem. Ber.*, 1942, **75**, 1830.

² Pigulevskii, G. V., and Kostenko, V. G., *Zh. obshch. Khim.*, 1960, **30**, 1057; *J. gen. Chem. USSR*, 1960, **30**, 1074.

³ Pigulevskii, G. V., Kostenko, V. G., and Kostenko, L. D., *Zh. obshch. Khim.*, 1961, **31**, 3143; *J. gen. Chem. USSR*, 1961, **31**, 2929.

⁴ Pigulevskii, G. V., Kostenko, V. G., and Kostenko, L. D., *Zh. obshch. Khim.*, 1962, **32**, 656; *J. gen. Chem. USSR*, 1962, **32**, 651.

⁵ Gray, P. S., and Mills, J. S., *J. chem. Soc.*, 1964, 5822.

⁶ Carman, R. M., *Aust. J. Chem.*, 1966, **19**, 629.

might have the structure antipodal to (I). The evidence for the structure supplied by earlier workers,^{3,5} which was based upon the reduction of abienol to (III) ($[\alpha]_D +1.5^\circ$; reported⁷ for authentic (III), $[\alpha]_D -1^\circ$), did not allow an absolute assignment of structure to be made. Consequently abienol has now been degraded to a compound of known absolute configuration and of large specific rotation.

Direct oxidation of abienol with osmium tetroxide and periodate, or with permanganate-periodate, gave a crystalline neutral compound, m.p. 122–123°. This compound, $C_{16}H_{22}O_2$, showed characteristic γ -lactone absorption in the infrared, and had an infrared spectrum superimposable upon that recorded⁸ for norambreinolide. A positive optical rotation indicated that the oxidation product was (+)-norambreinolide which has the known^{8,9} absolute configuration (VI). This evidence provides proof of the absolute configuration of abienol (I), and also for the relative stereochemistry at C8.

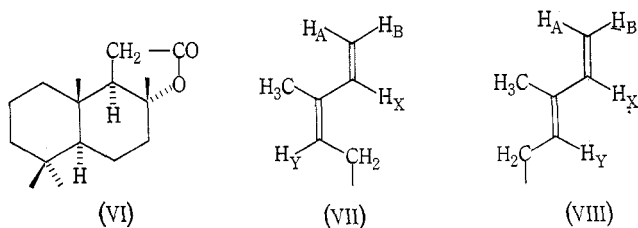


TABLE I

COMPARISON OF *cis* AND *trans* ISOMERSChemical shifts as τ values determined in CCl_4 , J in c/s, u.v. spectra in EtOH

Compound	H_A	H_B	H_X	H_Y	J_{AB}	λ_{max}	ϵ
Abienol (I, VII)	4.93	5.00	3.15	4.55	$\simeq 2$	238	19800
<i>cis</i> - α -Ocimene ¹¹ (VII)	4.96	5.03	3.35	4.77	1.8	234.5	21600
<i>cis</i> - β -Ocimene ¹¹ (VII)	4.89	4.97	3.27	4.72	1.8	237.5	21000
<i>cis</i> -Methyl communate ¹² (VII)	4.93	5.00	3.18	4.80		235	
<i>trans</i> -Methyl communate ¹⁰ (VIII)	4.98	5.15	3.72	4.60	1	232	27600
<i>trans</i> - α -Ocimene ¹¹ (VIII)	4.98	5.12	3.69	4.58	1.2	231	27300
<i>trans</i> - β -Ocimene ¹¹ (VIII)	5.00	5.13	3.70	4.61	1.2	232	27600

The proton magnetic spectrum of abienol confirms the gross structure (I) and provides evidence concerning the *cis* nature of the Δ^{12} double bond. The C12 proton occurs as a broad triplet at 4.55 τ ($J \simeq 7$ c/s) and the C15 and C16 protons occur as a seven-line ABX system (four X lines, three broad AB lines). The results of the analysis of this system are listed in Table 1. Results from similar systems

⁷ Hodges, R., and Reed, R. I., *Tetrahedron*, 1960, **10**, 71.⁸ Hinder, M., and Stoll, M., *Helv. chim. Acta*, 1953, **36**, 1995.⁹ Ruzicka, L., Seidel, C. F., and Engel, L. L., *Helv. chim. Acta*, 1942, **25**, 621.¹⁰ Norin, T., *Acta chem. scand.*, 1965, **19**, 1020.¹¹ Ohloff, G., Seibl, J., and Kováts, E., *Liebigs Ann.*, 1964, **675**, 84.¹² Thomas, B. R., private communication.

which have been tabulated in the literature,¹⁰⁻¹² and which have already been used to determine *cis/trans* isomerism in similar compounds (types VII and VIII), are also listed. The values for abienol, especially the value for the H_x proton which shows^{10,11} the greatest variation between *cis* and *trans* isomers, indicate that abienol almost certainly has the *cis* configuration (VII) rather than the *trans* structure (VIII). This view is supported by the peak position and intensity of the ultraviolet absorption of abienol⁵ (see Table 1).

With the absolute configuration and stereochemistry of abienol established as (I), the optical rotation of abienol (or alternatively of biformene and *trans*-communic acid)⁶ remains anomalous. However, the diterpenoids (II-V) with which abienol was compared do not have a *cis*- Δ^{12} double bond, nor do they have an 8- α -hydroxy- Δ^{12} -labdene system which could possibly form a hydrogen bond, and it may therefore be either of these features which causes the variation in optical rotation. It is hoped to check these views in the near future by synthesis of model compounds.

Experimental

Abienol (I)

Abienol was isolated from commercial Canada balsam (F. W. Berk & Co. Ltd, London) essentially as described by Gray and Mills,⁵ m.p. 40°, $[\alpha]_D +22^\circ$ (c, 0.9 in CHCl₃). The p.m.r. spectrum (CCl₄) showed 3.15 (C15; quartet), 4.55 (C12; broadened triplet), 4.93, 5.00 (C16; C16'; three broadened lines), 7.73 (C11; complex), 8.21 (C17 methyl, fine doublet; J 1 c/s), 8.88 (C14 methyl), 9.12, 9.17, 9.21 (C18, C19, C20 methyls) τ . ($J_{11,12}$ 7 c/s, $J_{15,16}$ 18 c/s, $J_{15,16'}$ 10 c/s, $J_{16,16'}$ 2 c/s.)

(+)-Norambreinolide (VI)

Abienol (2 g) in aqueous dioxan was treated with osmium tetroxide (0.1 g) and excess periodic acid. After 70 hr the flask containing a brown oil was worked up in the normal manner to give a trace of acidic material together with a neutral fraction. The neutral material, when chromatographed over alumina, gave, on elution with light petroleum, (+)-norambreinolide, m.p. 122-123° (after numerous recrystallizations from light petroleum and from methanol/water);* $[\alpha]_D +42^\circ$ (c, 0.25 in CHCl₃) (Found: C, 76.5; H, 10.3. Calc. for C₁₆H₂₆O₂: C, 76.75; H, 10.5%). The infrared spectrum was completely superimposable upon that recorded in the literature⁸ for authentic (+)-norambreinolide.

An attempt to purify the lactone by sublimation (75°/0.1 mm) resulted in decomposition to give crystals, m.p. 90-95°.

Abienol, on oxidation with permanganate/periodate in aqueous *t*-butanol under weakly alkaline conditions using the method of Von Rudloff,¹⁵ but requiring the occasional addition of further quantities of permanganate, gave (+)-norambreinolide, m.p. 122°, $[\alpha]_D +39^\circ$.

Acknowledgments

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* Literature values^{9,13,14} for (+)-norambreinolide, m.p. 122-125°, $[\alpha]_D +46^\circ$. The structure for this compound is incorrectly represented at C 8 in Simonsen, J., and Ross, W. C. J., "The Terpenes" Vol. V, pp. 602-3 (Cambridge University Press 1957).

¹³ Giles, J. A., and Schumacher, J. N., *Tetrahedron*, 1961, **14**, 246.

¹⁴ Stoll, M., and Hinder, M., *Helv. chim. Acta*, 1953, **36**, 1984.

¹⁵ Von Rudloff, E., *Can. J. Chem.*, 1956, **34**, 1413.