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82. J. D. Connolly,*1 Yoshio Kitahara,*2 K. H. Overton,*1 and Akira Yoshikoshi*2 : A Direct Correlation of Dolabradiene and Erythroxydiol Y.

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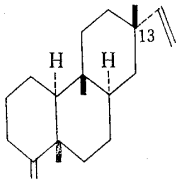
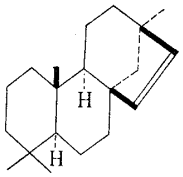
A series of recent papers[1~5] from our two laboratories have defined the structures and configurations of two antipodal pairs of diterpenoids : dolabradiene (I) and hibaene (II) from *Thujopsis dolabrata*, erythroxydiol Y (III) and the hydrocarbon (IV; R=R′=H) [and the related alcohols (IV; R or R′=OH, R′ or R=H)] from the botanically unrelated *Erythroxylon monogynum*.

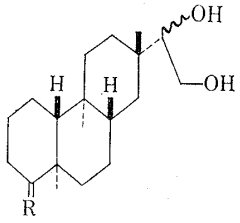
One notable conclusion was that both the tri- and tetracyclic diterpenoids from *Erythroxylon monogynum* had the same C-13 configurations, whereas the tri- and tetracyclic constituents of *Thujopsis dolabrata* were enantiomeric at C-13. Since hibaene (II) has been directly compared with isostevane[3] and the hydrocarbon (IV; R=R′=H) with stachene,[4] the C-13 configurations in the tetracyclic compounds cannot be in doubt. We have now effected a direct comparison between dolabradiene (I) and erythroxydiol Y (III), which confirms our previous conclusions that dolabradiene and hibaene are epimeric at C-13.



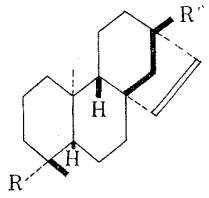
I



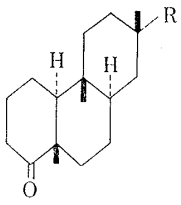
II



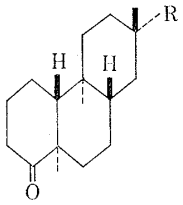
III : R=CH_2
VI : R=O



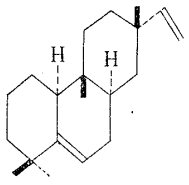
IV



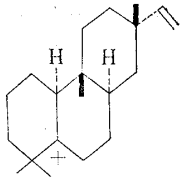
Va : R=CHO
VIIa : R=CH_3



Vb : R=CHO
VIIb : R=CH_3



VIII



IX

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4) R. D. H. Murray, R. McCrindle : Chem. & Ind. (London), **1964**, 500.
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We chose for comparison the C_{18} keto-aldehydes (Va, b). Dolabradiene had been previously converted[1] into Va by direct ozonolysis. Ozonolysis of the acetonide of erythroxydiol Y (III acetonide) afforded the nor-ketone acetonide (VI acetonide). Removal of the protective acetonide with aqueous acetic acid and alkaline hydrolysis of the resulting acetate afforded the keto-diol (VI), m.p. 139~141°, $[\alpha]_D$ +37°, which was cleaved to the keto-aldehyde (Vb) by sodium metaperiodate. This clearly differed (Table I) from the corresponding compound (Va) obtained from dolabradiene. Each keto-aldehyde was then converted into a mixture of mono- and bis-ethylene thioketals and these were without attempt at separation desulphurised with Raney nickel. Chromatography afforded in each case the monoketone (VIIa, b) as major product. The two ketones were identical by all criteria excepting the signs of their optical rotations (see Table I), demonstrating that they are enantiomeric and that therefore dolabradiene (I) and erythroxydiol Y (III) have the same configurations at C-13.

Table I. Physical Properties of the Keto-aldehydes and the Nor-ketones

	Dolabradiene (a)		Erythroxydiol Y (b)	
	m.p. (°C)	$[\alpha]_D$(°)	m.p. (°C)	$[\alpha]_D$(°)
Keto-aldehydes (Va,b)	112~113	−27	86~87	+51
Nor-ketones (VIIa,b)	83~85	−49	83~85	+54

Dolabradiene (I) and rimuene (VIII)[6] are thus close relatives, since the two hydrocarbons represent alternative fates of the hypothetical carbonium ion (IX).

Experimental

Nor-ketone (VIIb) from Erythroxydiol Y

Nor-ketone Acetonide (VI Acetonide)——Erythroxydiol Y acetonide (III acetonide)[5] (120 mg.) in ethyl acetate (10 ml.) was ozonised at −70° for 40 min. and the ozonide decomposed with zinc and acetic acid at 20°. Filtration and removal of acetic acid from the filtrate gave the nor-ketone acetonide (VI acetonide)[5] (100 mg.), rods from light petroleum, m.p. 138~140°, $[\alpha]_D$ +45°. *Anal.* Calcd. for $C_{22}H_{36}O_3$: C, 75.80; H, 10.41. Found: C, 75.70; H, 10.60.

Keto-diol (VI)——The above acetonide (VI acetonide) was kept in aqueous acetic acid (50%) for 4 hr. at 95°. Removal of the solvent *in vacuo*, followed by dissolution of the residue in boiling 5% ethanolic potassium hydroxide solution for 0.5 hr. to hydrolyse the resulting acetate, afforded the keto-diol (VI) (80 mg.), rods from ether-light petroleum, m.p. 139~142°, $[\alpha]_D$ +37°, $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (free OH), 3593 (bonded OH), 1711 (cyclohexanone). *Anal.* Calcd. for $C_{19}H_{32}O_3$: C, 73.98; H, 10.45. Found: C, 74.25; H, 10.70.

Keto-aldehyde (Vb)——The above keto-diol (VI) (30 mg.) in aqueous methanol (50%; 8 ml.) was treated with sodium metaperiodate (30 mg.; 1.5 equivalents) in water (5 ml.) at 0° for 2 hr. Addition of water (20 ml.) and extraction of the product into ether (3×10 ml.) gave on removal of solvent the keto-aldehyde (Vb), (25 mg.), leaflets from light petroleum, m.p. 86~87°, $[\alpha]_D$ +51°, $\nu_{max}^{CCl_4}$ cm^{-1}: 2700 and 1731 (aldehyde), 1712 (cyclohexanone), NMR signals at τ 0.54, 1H, singlet (aldehyde), τ 8.82, 8.88 and 9.13, 3H each, singlets (methyls). *Anal.* Calcd. for $C_{18}H_{28}O_2$: C, 78.20; H, 10.20. Found: C, 78.0; H, 10.20.

Keto-aldehyde (Va)[1]——The keto-aldehyde (Va), prepared as previously described,[1] m.p. 112~113°, $[\alpha]_D$ −27°, had NMR signals at τ 0.57, 1H, singlet (aldehyde); τ 8.87, 9.06 and 9.13, 3H each, singlets (methyls).

Nor-ketone (VIIb)——The keto-aldehyde (Vb) (45 mg.) was kept at 20° for 2 hr. in a mixture of freshly distilled ethane dithiol (0.2 ml.) and boron trifluoride-etherate (0.2 ml.). The ethereal solution was washed with 3*N* aqueous sodium hydroxyde (4×10 ml.) and the crude thioketal (40 mg.) [ν_{max} cm^{-1}: 1706 (cyclohexanone)] refluxed in acetone (AnalaR, 10 ml.) with an excess of Raney nickel for 16 hr. Filtration, extraction of the catalyst with hot acetone and removal of the solvent afforded a crude product (28 mg.), which crystallised spontaneously. Chromatography over silica gel gave (with light petroleum) a hydrocardon fraction (5 mg.) which was not further investigated. Elution with ether-light petroleum (1:19) gave the

6) J. D. Connolly, R. McCrindle, R. D. H. Murray, K. H. Overton: Tetrahedron Letters, **1964**, 1983.

nor-ketone (VIIb) (20 mg.), m.p. (sublimed at 0.1 mm.) 83~85°, $[\alpha]_D$ +54°, $\nu_{max}^{CCl_4}$ cm^{-1} : 1712 (cyclohexanone), NMR signals at τ 8.88, 9.11 and 9.19, 3H each, singlets (methyls). *Anal.* Calcd. for $C_{18}H_{30}O$: C, 82.38; H, 11.52. Found : C, 82.1; H, 11.4.

Nor-ketone (VIIa)——The keto-aldehyde (Va) (27 mg.) was reduced as above *via* the thioketal. Chromatography over silica gel afforded the nor-ketone (VIIa) (7 mg.), m.p. (sublimed at 0.1 mm.) 83~85°, $[\alpha]_D$ −49°. The IR and NMR spectra of this compound were indistinguishable from those of the nor-ketone (VIIb).

$[\alpha]_D$'s are in chloroform solution. NMR spectra are for deuteriochloroform solutions and were recorded on a Perkin-Elmer 60 Mc. Spectrometer.

Summary

It is proved by direct comparison that the nor-ketone (VIIa) derived from dolabradiene was enantiomeric with those (VIIb) from erythroxydiol Y. This is a further confirmation on configuration at C_{13} of dolabradiene and erythroxydiol Y.

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