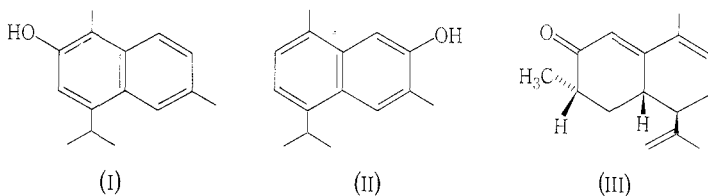


## 2-HYDROXY- AND 7-HYDROXY-CADALENE\*

By M. J. GALLAGHER† and M. D. SUTHERLAND‡

For determining the structures of isomeric cadinenes by the epoxide dehydrogenation method,<sup>1</sup> the ultraviolet spectra of 2-hydroxy- and 7-hydroxy-cadalene were required in addition to those already reported for cadalene<sup>2</sup> and 5-hydroxy-cadalene.<sup>2</sup>



Although 2-hydroxycadalene (I) had already been prepared from 2-nitrocadalene,<sup>3,4</sup> we preferred to use 2-bromocadalene for which different melting points have been reported by Gripenberg<sup>3</sup> (m.p. 52–52.5°) and by Briggs *et al.*<sup>4</sup> (m.p. 39°). We were able to obtain samples of both dimorphs and to interconvert them. The bromo compounds, although reluctant to form a Grignard compound in tetrahydrofuran, reacted with magnesium in boiling tributyl borate to form a boronic acid<sup>5</sup> which was oxidized with hydrogen peroxide<sup>6</sup> to 2-hydroxycadalene, identical with Gripenberg's naphthol.<sup>3</sup>

7-Hydroxycadalene (II) was obtained by the sequence used by Briggs *et al.*<sup>4</sup> but starting with (+)-carvone in place of carvotanacetone. An interesting intermediate, (+)-4,4a,5,6-tetrahydro-5-isopropenyl-3,8-dimethyl-3H-naphthalen-2-one, was obtained in crystalline form and is presumably (III) rather than a mixture of diastereoisomers, in consequence of base-catalysed equilibration during the saponification of the ester. Some  $\beta$ -hydroxyketone ( $\nu(\text{CO})$  1725  $\text{cm}^{-1}$ ), analogous to the principal product obtained by Briggs *et al.*,<sup>4</sup> remained in the mother liquors of (III). Dehydrogenation of the ketone with palladized charcoal yielded 7-hydroxycadalene in 58% yield.

The ultraviolet spectra of both naphthols are reproduced in Figure 1 in view of their utility in the structural investigation of the cadinenes, muurolenes, etc.

\* Manuscript received January 12, 1965.

† Chemistry Department, University of Queensland, Brisbane; present address: Chemistry School, University of New South Wales.

‡ Chemistry Department, University of Queensland, Brisbane.

<sup>1</sup> Gallagher, M. J., Hildebrand, R. P., and Sutherland, M. D., *Tetrahedron Letters*, 1964, 3715.

<sup>2</sup> Hildebrand, R. P., and Sutherland, M. D., *Aust. J. Chem.*, 1959, **12**, 678.

<sup>3</sup> Gripenberg, J., *Annls. Acad. Sci. Fenn. A*, 1943, 59 (14), 7; Elsevier, "Encyclopaedia of Organic Compounds." Vol. 12B, p. 1432. (Elsevier: Amsterdam 1950.)

<sup>4</sup> Briggs, L. H., Gill, N. S., Lions, F., and Taylor, W. I., *J. Chem. Soc.*, 1949, 1098.

<sup>5</sup> Cowrie, W. P., Jackson, A. H., and Musgrave, O. C., *Chem. & Ind.*, 1959, 1248.

<sup>6</sup> Hawthorne, M. F., *J. Org. Chem.*, 1957, **22**, 1001.

*Experimental**Cadalene*

The sesquiterpene fraction of cade oil was repeatedly worked for cadinene dihydrochloride until exhausted. The mother liquors (300 ml) and sulphur (180 g) were boiled under reflux for 30 min, cooled, steam-distilled, and the steam-volatile oil fractionated in a 20-plate-equivalent still to yield gas chromatographically pure cadalene, b.p. 153.5–154°/10 mm (80 ml). Longer periods of refluxing<sup>4</sup> yielded an inhomogeneous product, which could not be completely purified even through the picrate.

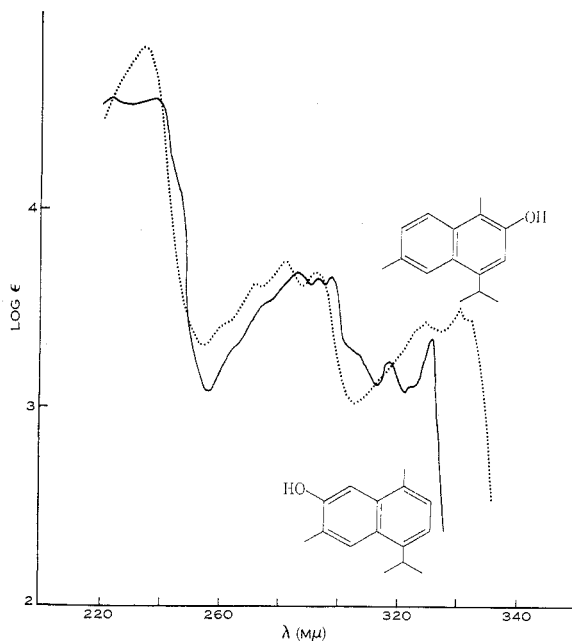


Fig. 1

*2-Bromocadalene*

This was prepared from cadalene by the method of Briggs *et al.*<sup>4</sup> as needles, m.p. 51.5–52.5°, from methanol or ethyl acetate. Low temperature recrystallization from methanol gave small prisms, m.p. 38–39°, convertible to the higher melting form by heating or slowly on keeping at room temperature. Both forms yielded the known<sup>4</sup> picrate, m.p. 114–115°, and trinitrobenzolate, m.p. 125–126°.

*2-Hydroxycadalene*

2-Bromocadalene (36.3 g), tri-*n*-butyl borate (65 g), and magnesium (3.1 g) were refluxed together under nitrogen (5 hr), cooled, dissolved in 10% hydrochloric acid, and extracted with ether (200 ml). The ethereal extract, after being washed twice with water, was brought to the boil and held there by the dropwise addition of 100 ml of 10% hydrogen peroxide. Phenolic material was recovered with Claisen's alkali and heated in a small still till the stillhead temperature reached 140°/1 mm. The residue was steam-distilled under an oil trap containing isooctane, which was removed periodically and evaporated to yield 3.1 g of 2-hydroxycadalene, needles, m.p. 76.5–77.5° from light petroleum (Found: C, 84.0; H, 8.65. Calc. for C<sub>18</sub>H<sub>18</sub>O: C, 84.1;

H, 8.4%). The naphthol, which discoloured at room temperature, was stable at 6° and gave the reported<sup>3</sup> picrate (m.p. 141–142°), and trinitrobenzoate (m.p. 149.5–150°).

The ultraviolet absorption spectrum was measured in isooctane solution using a Spectracord 4000A and showed  $\lambda_{\max}$  234 m $\mu$  (log 4.83), 271 (3.62), 281 (3.74), 292 (3.69), 329 (3.43), 340 (3.50);  $\lambda_{\min}$  254 m $\mu$  (3.30), 274 (3.61), 287 (3.61), 306 (3.03), 334 (3.38);  $\lambda_{\text{inf}}$  264 m $\mu$  (3.45); 325 (3.39); and 343 (3.45).

(+)-4,4a,5,6-Tetrahydro-5-isopropenyl-3,8-dimethyl-3H-naphthalen-2-one

(+)-Carvone (25.4 g,  $[\alpha]_D^{25} + 47^\circ$ ), morpholine hydrochloride (22 g), trioxymethylene (1.7 g), and absolute ethanol (20 ml) were refluxed together with half-hourly additions of 1.7 g of trioxymethylene to a total of 6.8 g. After a further 2 hr of refluxing, the reaction mixture was diluted with water, ether extracted to remove unreacted carvone, made basic with sodium hydroxide (7 g), and thoroughly extracted with ether. Removal of the ether left the Mannich base (29.3 g) as a dark oil which was treated with methyl iodide (23 g) in anhydrous ether for 48 hr at 6°. Evaporation left crude methiodide (39 g), which was dissolved in a solution of sodium (3.8 g) and ethyl  $\alpha$ -methyl acetoacetate (23.7 g) in absolute ethanol (80 ml) and boiled under reflux for 3.5 hr. The reaction mixture was then refluxed for 5 hr with potassium hydroxide (10 g) in water (20 ml). After the removal of the bulk of the ethanol and the addition of water, the crude ketone (19.8 g) was isolated by ether extraction. Distillation through a short column gave a fraction, b.p. 130–150°/1 mm (11.3 g), which partly crystallized on cooling. Low temperature recrystallization from ethanol gave the pure ketone m.p. 70–72°,  $[\alpha]_D^{21} + 80.8^\circ$  (c. 2.6 in  $\text{CHCl}_3$ ) (Found: C, 83.1; H, 9.1.  $\text{C}_{18}\text{H}_{20}\text{O}$  requires C, 83.3; H, 9.2%).  $\lambda_{\max}$  (isooctane) 272 m $\mu$ , log  $\epsilon_{\max}$  4.37,  $\nu(\text{CO})$  1670  $\text{cm}^{-1}$ ,  $\nu(\text{CH})$  893, 822, 830  $\text{cm}^{-1}$  (Nujol mull).

The 2,4-dinitrophenylhydrazone, m.p. 173–175° (Found: C, 63.6; H, 6.3; N, 14.1.  $\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}_4$  requires C, 63.6; H, 6.1; N, 14.1%), formed red needles from ethanol. The semicarbazone showed m.p. 195.8–196.5° (decomp.) from ethanol (Found: C, 70.3; H, 8.8; N, 15.0.  $\text{C}_{18}\text{H}_{23}\text{N}_3\text{O}$  requires C, 70.3; H, 8.4; N, 15.4%).

7-Hydroxycadalene

Distilled ketone (5.97 g) and 10% palladized charcoal (2 g) were heated at 200° in a stream of nitrogen for 1 hr. Steam-distillation under an oil trap containing isooctane yielded 7-hydroxycadalene (3.43 g) as a felt-like mass of crystals, m.p. 115–116°, from the cooled isooctane. Recrystallization from light petroleum yielded the pure naphthol, m.p. 118–119.5° (Found: C, 83.9; H, 8.3. Calc. for  $\text{C}_{18}\text{H}_{18}\text{O}$ : C, 84.1; H, 8.4%) which yielded the known<sup>4</sup> picrate, m.p. 138.5–139.5°, and trinitrobenzoate, m.p. 139–140°.

The ultraviolet absorption spectrum in isooctane showed  $\lambda_{\max}$  222 m $\mu$  (log  $\epsilon$  4.56), 238 (4.56), 285 (3.68), 293 (3.64), 297 (3.65), 317 (3.26), 331 (3.34);  $\lambda_{\min}$  255 m $\mu$  (3.09), 290 (3.62), 295 (3.62), 312 (3.13), 322 (3.09);  $\lambda_{\text{inf}}$  266 m $\mu$  (3.32), 275 (3.53), 304 (3.30).