Synthetic Experiments in the Eremophilane Sesquiterpene Group. Synthesis of (±)-7-*epi*-Nootkatone and Partial Synthesis of Valerianol. The Structure of Nardostachone

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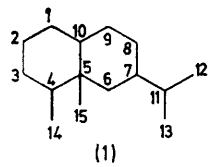
Although the Robinson annelation of *cis*-4-isopropenyl-2-methylcyclohexanone with *trans*-pent-3-en-2-one affords (±)-nootkatone [4β*H*,5α-eremophila-1(10),11-dien-2-one] in low yield, the major product is (±)-7-*epi*-nootkatone. The stereochemical composition of the product appears to be very sensitive to the reaction conditions. A partial synthesis of natural (+)-valerianol [4β*H*,5α-eremophil-1(10)-en-11-ol] from (+)-nootkatone is described. The structure (15) assigned to nardostachone must be revised, since 4β*H*,5α-eremophila-1(10),8-dien-2-one (15) synthesised unequivocally from natural nootkatone is not identical with the natural material.

INTEREST in the eremophilane family of bi- and tricyclic sesquiterpenes has increased of late, owing to the discovery during the past few years of several new members. The compounds, which have been found to be widely distributed in nature, now number about 40.[1] Several groups have directed attention towards the synthesis of these sesquiterpenes, which are characterised by the non-isoprenoid carbon framework (1), and a few of the newer members (as their racemic varieties) have now been synthesised.[2,3] Hydroxyeremophilone, one of the original trio of eremophilanoid sesquiterpenes, has recently been totally synthesised as the natural (+)-form.[3] We describe here some of our own further synthetic studies in this area.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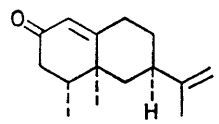
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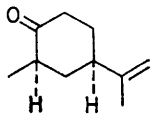
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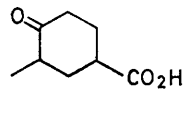
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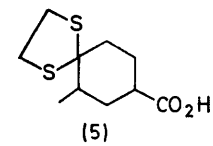
Nootkatone [4βH,5α-*Eremophila*-1(10),11-*dien*-2-*one*]. —Several syntheses [2e,h,j] of the racemic variety of this ketone (2),† the (+)-form of which occurs in grapefruit oil [4] and in the heartwood of Alaska yellow cedar,[5] have been reported recently. We envisaged a synthesis involving annelation of *cis*-4-isopropenyl-2-methylcyclohexanone (*cis*-dihydrosylvecarvone) (3) with *trans*-pent-3-en-2-one.[6] The former ketone was made from diethyl malonate, which by a well-documented synthesis was converted into 3-methyl-4-oxocyclohexanecarboxylic acid (4),[7,8] Protection of the keto-group in structure (4) by acetal formation with ethylene glycol proved to be unsatisfactory, owing to some interaction between the glycol and the carboxy-group. However the compound formed a dithioacetal (5) smoothly on treatment with ethanedithiol. Treatment of the acetal (5) with methyllithium [9] yielded the methyl ketone (6), which in a Wittig reaction with methylenetriphenylphosphorane [10] was converted into the olefin (7). Hydrolysis [11] of the latter gave *cis*-4-isopropenyl-2-methylcyclohexanone (3), the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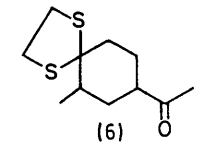
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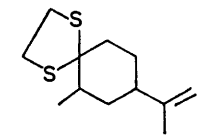
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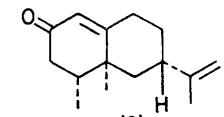

(8)

stereochemistry being assigned on the presumption that the alkyl and alkenyl groups are both equatorial.

† Formulae (2), (9)—(18), and (20) represent, either wholly or in part, a single enantiomers. The others, when asymmetry exists, are enantiomeric pairs.

[1] For a recent review, see A. R. Pinder, *Perfumery Essent. Oil Record*, 1968, **59**, 280, 645.

[2] See, *inter al.*, (*a*) J. A. Marshall, H. Faubl, and T. M. Warne, *Chem. Comm.*, 1967, 753; (*b*) C. Berger, M. Franck-Neumann, and G. Ourisson, *Tetrahedron Letters*, 1968, 3451; (*c*) R. M. Coates and J. E. Shaw, *ibid.*, 1968, 5405; *Chem. Comm.*, 1968, 515; *J. Amer. Chem. Soc.*, 1970, **92**, 5657; (*d*) R. M. Coates and J. E. Shaw, *J. Org. Chem.*, 1970, **35**, 2597; (*e*) M. Pesaro, G. Bozzato, and P. Schudel, *Chem. Comm.*, 1968, 1152; (*f*) E. Piers and R. J. Keziere, *Canad. J. Chem.*, 1969, **47**, 137; (*g*) E. Piers, R. W. Britton, and W. de Waal, *ibid.*, p. 831; (*h*) J. A. Marshall and R. A. Ruden, *Tetrahedron Letters*, 1970, 1239; *J. Org. Chem.*, 1971, **36**, 594; (*i*) J. A. Marshall and G. M. Cohen, *Tetrahedron Letters*, 1970, 3865; *J. Org. Chem.*, 1971, **36**, 877; E. Piers and R. D. Smillie, *ibid.*, 1970, **35**, 3997; (*j*) A. van der Gen, L. M. van der Linde, J. G. Witteveen, and H. Boelens, *Rec. Trav. chim.*, 1971, **90**, 1034, 1045; (*k*) E. Piers, M. B. Geraghty, and R. D. Smillie, *Chem. Comm.*, 1971, 614.

[3] A. R. Pinder and A. K. Torrence, *J. Chem. Soc.* (*C*), 1971, 3410.

[4] W. D. MacLeod, jun., and N. M. Buigues, *J. Food. Sci.*, 1964, **29**, 565; W. D. MacLeod, jun., *Tetrahedron Letters*, 1965, 4779.

[5] H. Erdtman and Y. Hirose, *Acta Chem. Scand.*, 1962, **16**, 1311.

[6] H. C. Odom, jun., and A. R. Pinder, *Org. Synth.*, 1971, **51**, 115.

[7] H. A. Bruson and T. W. Riener, *J. Amer. Chem. Soc.*, 1943, **65**, 23.

[8] P. Sengupta, *J. Org. Chem.*, 1953, **18**, 249.

[9] For a review, see M. J. Jorgenson, *Org. Reactions*, 1970, **18**, 1.

[10] *Cf.* G. Wittig and U. Schoellkopf, *Org. Synth.*, 1960, **40**, 66.

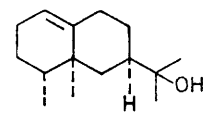
[11] *Cf.* D. Seebach, N. R. Jones, and E. J. Corey, *J. Org. Chem.*, 1968, **33**, 300.

The annelation of compound (3) was effected with sodium hydride as base. On the first occasion we performed this experiment, we were able,[12] after a tedious sequence of purification steps, to isolate a very low yield of a crystalline product, m.p. 45—46°. Comparison of this (u.v. spectra i.r. spectra in solution, g.l.c., and t.l.c.) with natural (+)-nootkatone suggested that it was (±)-nootkatone; this was confirmed by comparisons (capillary g.l.c. and mixed m.p.) with an authentic sample of (±)-nootkatone synthesised by Schudel *et al.*,[2e] by a different route. However, we have not been able to reproduce this result *in toto*. Subsequent annelations have yielded a liquid product containing 10—20% nootkatone (capillary g.l.c. evidence *), the major product being 7-*epi*-nootkatone (8).[2j] Although we have not studied this reaction closely, it seems clear that the stereochemical composition of the product is sensitive to the reaction conditions. Several workers have shown that this is the case in annelations of other cyclohexanones or their enamines with *trans*-pent-3-en-2-one.[14]

The u.v. and i.r. spectral properties, and the g.l.c. and t.l.c. behaviour of nootkatone and 7-*epi*-nootkatone are almost identical, but the epimers can be distinguished by capillary g.l.c. and by their n.m.r. spectra, which show small but significant chemical shift differences.[2j] The n.m.r. spectrum of our liquid product was virtually identical with that of the product obtained by van der Gen *et al.*,[2j] who, some time after our preliminary report,[12] effected the same annelation, using triphenylmethylsodium as base; these authors did not detect any (±)-nootkatone (by n.m.r. analysis) in their product. We found no evidence (n.m.r. and g.l.c. analysis) of the presence of 4,5-*trans*-dimethyl epimerides in our product.

Valerianol [4βH,5α-*Eremophil*-1(10)-*en*-11-*ol*].—The (+)-form of this alcohol occurs in the essential oil of the roots of *Valeriana officinalis* L.,[15] and in camphor blue oil.[16] Degradation and spectroscopic study have culminated in assignment of structure (9) to (+)-valerianol.[15,16] We describe here a confirmation of the structure and absolute configuration by a partial synthesis from (+)-nootkatone. After the completion of this work a total synthesis of (±)-valerianol was described.[2d]

(+)-Nootkatone (2) was epoxidised selectively to 11,12-epoxy-11,12-dihydronootkatone (10) with *m*-chloroperbenzoic acid. The product crystallized readily and was presumably one of the two possible epimerides. Reduction with lithium aluminium hydride yielded the diol (11) as a mixture of epimerides, which was selectively acetylated give to the monoacetate (12). This product



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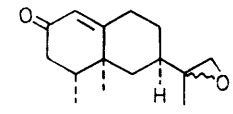

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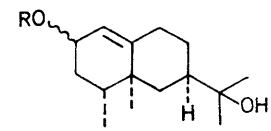
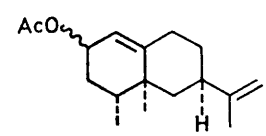


(11) R = H
(12) R = Ac

was accompanied, on i.r. evidence, by a small amount of the diene (13). Hydrogenolysis of the acetate (12) with lithium in liquid ammonia gave, after preparative g.l.c. purification (+)-valerianol (9), identical with an authentic sample.



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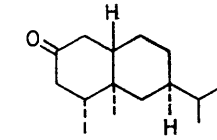

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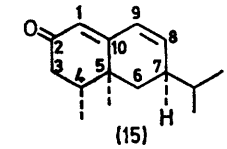

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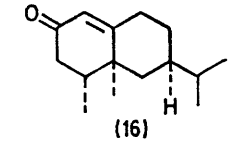


(16)

Nardostachone.—The (+)-modification of this ketone is a constituent of Indian spikenard oil (*Nardostachys jatamansi* D.C.).[17,18] On hydrogenation it affords tetrahydronootkatone (14), and on this and spectral evidence the structure and stereochemistry (15) have been advanced for the compound.[17,18] However, the reported u.v. absorption maximum [298 nm in ethanol (ε 15,200)] is not consonant with this formulation, on the basis of Woodward's rules[19] [$\lambda_{max.}$ (calc.) 280 nm]. Further, the observed maximum for the semicarbazone (317 nm)[17] is at variance with structure (15) for the ketone. Compound (15) has therefore been synthesised unequivocally as follows. Selective hydrogenation of (+)-nootkatone by homogeneous catalysis[20] led to

* Dr. P. Schudel has informed us[13] that his group has synthesised all the possible racemates corresponding to structure (2) except 7-*epi*-nootkatone (8). Two of these, nootkatone and 4-*epi*-nootkatone are described in ref. 2*e*. The third will be described in a forthcoming publication.

[12] H. C. Odom, jun., and A. R. Pinder, *Chem. Comm.*, 1969, 26.

[13] P. Schudel, personal communication.

[14] R. M. Coates and J. E. Shaw, *Chem. Comm.*, 1968, 47; R. L. Hale and L. H. Zalkow, *ibid.*, p. 1249; J. A. Marshall and T. M. Warne, *J. Org. Chem.*, 1971, **36**, 178; C. J. V. Scanio and R. M. Starrett, *J. Amer. Chem. Soc.*, 1971, **93**, 1539.

[15] G. Jommi, J. Krepinsky, V. Herout, and F. Šorm, *Tetrahedron Letters*, 1967, 677; *Coll. Czech. Chem. Comm.*, 1969, **34**, 593.

[16] H. Hikino, N. Suzuki, and T. Takemoto, *Chem. and Pharm. Bull. (Japan)*, 1968, **16**, 832.

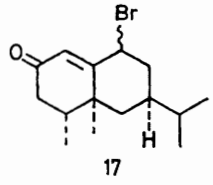
[17] S. D. Sastry, M. L. Maheswari, K. K. Chakravarti, and S. C. Bhattacharyya, *Perfurmery Essent. Oil Record*, 1967, **58**, 154.

[18] S. D. Sastry, M. L. Maheswari, K. K. Chakravarti, and S. C. Bhattacharyya, *Tetrahedron*, 1967, **23**, 2491.

[19] R. B. Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 76.

[20] *Cf.* M. Brown and L. W. Piszkiewicz, *J. Org. Chem.*, 1967, **32**, 2013.

11,12-dihydronootkatone (16), which had $\lambda_{max.}$ (EtOH) 238 nm, and showed no C=CH_2 band (*ca.* 890 cm^{-1}) in its i.r. spectrum. Treatment of the ketone (16) with *N*-bromosuccinimide yielded the 9-bromoketone (17), which was not purified but was dehydrobrominated directly by heating with γ-collidine. One mol. equiv. of collidine hydrobromide was formed, along with a homogeneous (t.l.c. and g.l.c.) ketone, $\lambda_{max.}$ (EtOH) 283 nm (ε 18,500), formulated on analytical and spectral evidence as 4β*H*,5α-eremophila-1(10),8-dien-2-one (15). The n.m.r. spectrum of this product in the olefinic proton region was unusually simple: two signals only were apparent, at δ 6·2 [2H, s, C(8)H and C(9)H] and 5·7 p.p.m. [1H, s, slight evidence of splitting, C(1)H]. This spectrum is very different in the low-field region from the published spectrum of nardostachone.[17,18] Further, the synthetic product formed a semicarbazone of m.p. 213° (decomp.), $\lambda_{max.}$ (EtOH) 297·5 nm (ε 24,100).



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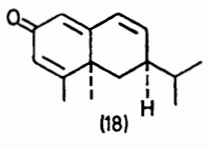

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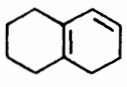
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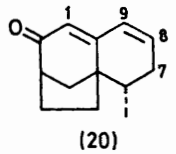

(20)

whereas nardostachone semicarbazone has m.p. 230—232° (decomp.); on admixture the synthetic and 'natural' compounds showed a large m.p. depression. It is apparent that structure (15) cannot represent nardostachone. A reappraisal of the published details[17,18] suggests that it might be better formulated as the cross-conjugated trienone 5α-eremophila-1(10),3,8-trien-2-one (18) (Found:[18] C, 82·6; H, 9·75. $C_{15}H_{20}O$ requires C, 82·3; H, 9·3%. Semicarbazone: found: C, 70·05; H, 8·9; N, 15·4. $C_{16}H_{12}N_3O$ requires C, 70·3; H, 8·5; N, 15·4%). U.v. maxima for structure (18) would be expected in the 220, 250, and 300 (principal) nm regions.[21] The natural ketone is reported[17,18] to have a subsidiary maximum at 232 nm. However, the new structure is not entirely reconcilable with the published n.m.r. spectrum.[18] The simplicity of the n.m.r. spectrum of compound (15) in the low-field region suggests that the C-8 and C-9 protons have the same chemical shift and are therefore not coupled. The absence of coupling between them and the allylic proton at C-7 is explicable in terms of an almost 90° dihedral angle between the olefinic C–H bonds and the allylic C–H bond. Examples for comparison include structures (19), exhibiting but a single =C–H signal,[22] and (20), which shows a singlet at δ 5·5 [C(1)H] and a doublet at 6·1 [C(8)H and C(9)H, coupled to one C(7)H (*J* 2 Hz)].[23]

[21] For analogues in the steroid field for comparison, see C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann, and J. Pataki, *J. Amer. Chem. Soc.*, 1950, **72**, 4534.

EXPERIMENTAL

Comparisons by capillary g.l.c. were made either on a 20 m × 0·3 mm (int. diam.) open tubular column coated with OV-101 (methyl silicone liquid polymer) at 125°, or on a 50 m × 0·4 mm (int. diam.) column coated with Triton X-305 (polyethylene glycol + polyoxymethylene) at 220°. Helium was used as carrier gas.

4,4-Ethylenedithio-3-methylcyclohexanecarboxylic Acid (5).—3-Methyl-4-oxocyclohexanecarboxylic acid (4·68 g) (synthesised[7,8] from diethyl malonate) in acetic acid (75 ml) was mixed with ethanedithiol (2·82 g, 1 mol. equiv.) and boron trifluoride–ether complex (4·5 ml). After being stirred at room temperature for 20 h the mixture was poured into a large amount of ice–water and the *dithioacetal* was isolated with ether. The product was distilled (b.p. 168° at 0·25 mmHg; yield 6·0 g), and slowly solidified; m.p. 84°; δ 1·20 (3H, d, *J* 8 Hz), 1·85 (8H, m), 3·35 (4H, s), and 11·86 (1H, s) (Found: C, 52·0; H, 7·0; S, 27·9. $C_{10}H_{16}O_2S_2$ requires C, 51·7; H, 6·9; S, 27·6%).

4,4-Ethylenedithio-3-methylcyclohexyl Methyl Ketone (6).[9]—The preceding carboxylic acid (23·2 g, 0·1 mol) in dry ether (200 ml) was added gradually, with stirring, to ethereal methyl-lithium (1·95M; 105 ml, 0·2 mol) cooled in ice, during 1 h. The mixture was stirred several hours longer, then treated with ice–water until the system separated into two clear layers. The aqueous layer was extracted twice with ether and the combined organic layers were washed with sodium hydrogen carbonate solution, dried, and concentrated. Removal of the solvent left the *methyl ketone*, which was distilled (b.p. 117—118° at 0·03 mmHg; yield 18·6 g, 80%); $\nu_{max.}$ (film) 1695 cm^{-1} (no OH band); δ 1·10 (3H, d, *J* 8 Hz), 2·11 (3H, s), and 3·28 (4H, s) (Found: C, 57·2; H, 8·0; S, 28·0. $C_{11}H_{18}OS_2$ requires C, 57·4; H, 7·9; S, 27·8%).

1,1-Ethylenedithio-4-isopropenyl-2-methylcyclohexane (7).[10]—Methyltriphenylphosphonium bromide (3·9 g, 0·011 mol) was added all at once, under nitrogen, to a stirred solution of butyl-lithium in hexane (1·6M; 7 ml, 0·012 mol) diluted with dry ether (50 ml). Stirring was continued for 4 h, then a solution of the foregoing ketone (2·3 g, 0·01 mol) in dry ether (10 ml) was added dropwise during 15 min, with continued stirring overnight. The mixture was cooled and decomposed with ice–water, and the organic layer was separated, dried, and concentrated. The residue was taken up in light petroleum (b.p. 30—60°) and passed down a column of alumina, with the same solvent as eluant. Evaporation of the eluate yielded the *alkene*, b.p. 115—117° at 0·08 mmHg (2·0 g, 88%); $\nu_{max.}$ (film) 898 cm^{-1} (C=CH_2) (no C=O band); δ 1·10 (3H, d, *J* 8 Hz), 1·71 (3H, s), 3·20 (4H, s), and 4·70br (2H, s) (Found: C, 63·25; H, 9·0; S, 28·0. $C_{12}H_{10}S_2$ requires C, 63·1; H, 8·8; S, 28·1%).

cis-*4-Isopropenyl-2-methylcyclohexanone* [(±)-cis-*Dihydrosylvecarvone*] (3).[11]—A mixture of the preceding olefin (4·56 g), mercury(II) chloride (11·4 g), mercury(II) oxide (3·38 g), water (15 ml), and methanol (250 ml) was refluxed on a water-bath for 4 h under nitrogen. Inorganic matter was filtered off and the filtrate was diluted with three

[22] R. B. Bates, R. H. Carnighan, and C. E. Staples, *J. Amer. Chem. Soc.*, 1963, **85**, 3030.

[23] J. A. Marshall and S. F. Brady, *Tetrahedron Letters*, 1969, 1387.

volumes of ice–water, and extracted thrice with methylene chloride. The combined extracts were washed with saturated aqueous ammonium chloride, then water, dried, and concentrated. The residual *ketone* was distilled (b.p. 120° at 40 mmHg; yield 2·1 g, 70%); $\nu_{max.}$ (film) 1701 (C=O) and 888 cm^{-1} (C=CH_2); δ 0·95 (3H, d, *J* 6 Hz), 1·75 (3H, s), and 4·75 (2H, s) (Found: C, 78·7; H, 10·6. $C_{10}H_{16}O$ requires C, 78·9; H, 10·6%). The spectral parameters agree with those reported by van der Gen *et al.*,[2j] and with those for the (−)-enantiomer reported by Ohloff and Giersch.[24]

Annelation of (±)-cis-*Dihydrosylvecarvone* (3) *with* trans-*Pent-3-en-2-one*.—Sodium hydride (50% dispersion in mineral oil; 5·5 g, 0·115 mol) was washed thrice by decantation with light petroleum (b.p. 30—60°), then suspended in dry ether (100 ml) and stirred at 0° under nitrogen. The foregoing ketone (8·5 g, 0·056 mol) in dry ether (50 ml) was then added gradually during several min, and the mixture stirred for 5·5 h, the temperature gradually rising to that of the room. The mixture was once more cooled in ice and stirred during the addition of *trans*-pent-3-en-2-one [6] (9·4 g, 0·056 mol) in dry ether (50 ml) (5 min), then stirred for 60 h at room temperature. Ice-cooling was again applied during the careful addition of ice–water until decomposition was complete. The organic layer was separated and the aqueous layer extracted twice with ether. The combined ethereal extracts were washed with water, dried, and concentrated, yielding a yellow oil (14·8 g), which was subjected to fractional distillation (3·5 in vacuum-jacketed Vigreux column). Two fractions were separated: (*a*) b.p. 100—110° at 0·05 mmHg (7·8 g), mainly unchanged dihydrosylvecarvone, and (*b*) b.p. 110—125° at 0·05 mmHg (2·1 g), the i.r. spectrum of which showed bands due to OH, saturated C=O, αβ-unsaturated C=O, and C=CH_2 groups. This fraction was refluxed on a water bath for 10 h with methanolic 5% potassium hydroxide (30 ml), under nitrogen, then stripped of most of the solvent *in vacuo* and diluted with a large volume of ice–water. Extraction with ether (thrice) gave a yellow oil (2·0 g) (virtually no OH or saturated C=O bands in i.r.), which was subjected, in light petroleum (50 ml; b.p. 30—60°) solution, to chromatography on alumina (column 9 × 1 in diam.; Merck), with the same solvent (13 × 50 ml) as eluant. Fractions were monitored by i.r. spectroscopy; nos. 3—13 were combined and concentrated. The residue (0·87 g) was rechromatographed from light petroleum (b.p. 30—60°) on Baker 0537 alumina (column 7 × 1 in diam.), and eluted with the same solvent (18 × 100 ml). Fractions 10—18 were concentrated, and the residue distilled [b.p. 120° (bath) at 0·01 mmHg; yield 0·42 g]; $\lambda_{max.}$ (EtOH) 241 nm (ε 11,300); $\nu_{max.}$ (film) 1672 (C=O), 1626 (C=C), and 889 cm^{-1} (C=CH_2) [spectrum indistinguishable from that of natural or (±)-nootkatone]; δ 0·90 (3H, d, poorly resolved), 1·10 (3H, s), 1·75 (3H, s), 4·75 (2H, s), and 5·83 (1H, s). The n.m.r. spectrum showed differences from that of authentic nootkatone, and was virtually identical with that of 7-*epi*-nootkatone.[2j] G.l.c. on a 20 ft 25% Carbowax on Chromosorb W column at 230° showed a single peak, coincident with that of natural or (±)-nootkatone; however, g.l.c. on a 20 m OV-101 glass capillary column showed that the product was about 90% 7-*epi*-nootkatone and 10% nootkatone. T.l.c. showed a single spot, also coincident with that of the nootkatones (Found: C, 82·7; H, 10·0. Calc. for $C_{15}H_{22}O$: C, 82·6; H, 10·1%).

11,12-*Epoxy*-11,12-*dihydronootkatone* [11,12-*Epoxy*-4βH,5α-*eremophil*-1(10)-*en*-2-*one*] (10).—Natural (+)-nootkatone (0·5 g) in dry chloroform (15 ml) was treated with *m*-chloroperbenzoic acid (85%; 0·46 g) and the mixture was kept in the refrigerator overnight. It was diluted with ether, washed with dilute aqueous sodium hydroxide and brine, dried, and concentrated. The residual *epoxy-ketone* was distilled [b.p. 160° (bath) at 0·1 mmHg; yield 0·5 g]; the distillate solidified quickly and crystallised from light petroleum (b.p. 60—90°) in needles, m.p. 92°; $\nu_{max.}$ ($CHCl_3$) 1645 (C=O), 1610 (C=C), and 1274 cm^{-1} (epoxide) [no band at 885—895 cm^{-1} (C=CH)]; δ 1·09 (3H, d, *J* 7 Hz), 1·28 (3H, s), 2·20 (3H, d, *J* 5 Hz), 2·62 (2H, d, *J* 4 Hz), and 5·72 (1H, s) (Found: C, 76·7; H, 9·5. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%).

Reduction of 11,12-*Epoxy*-11,12-*dihydronootkatone*.—The foregoing epoxy-ketone (0·5 g) in dry ether (20 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (0·3 g) in dry ether (25 ml) at 0—5°, during 15 min. The mixture was stirred at room temperature for a further 7 h, then decomposed by cautious addition of ice–water in the presence of Celite. The ethereal solution was decanted, and the residue washed several times with ether. The combined extract and washings were dried, and the solvent was removed. 4β*H*,5α-Eremophil-1(10)-ene-2,11-diol (11) remained as a viscous syrup (mixture of epimers) which was distilled [b.p. 165° (bath) at 0·2 mmHg; yield 0·5 g); $\nu_{max.}$ (film) 3390 cm^{-1} (OH) (no C=O or epoxide bands); δ 0·99 (6H, m), 1·13 (6H, s), 3·40—4·30 (2H, m), and 5·31 (1H, s) (Found: C, 75·6; H, 11·0. Calc. for $C_{15}H_{26}O_2$: C, 75·6; H, 10·9%).

Acetylation of the Diol (11).—The diol (0·43 g), pyridine (5 ml), and acetic anhydride (0·53 g) were mixed and kept at 0° for 24 h, with occasional agitation. The solution was poured into an excess of ice-cold dilute hydrochloric acid and the product isolated with ether. The 2-*acetate* (12) (mixture of epimers) was distilled [b.p. 140—145° (bath) at 0·08 mmHg; yield 0·45 g); a small fore-run consisted largely of the diene (13)]; $\nu_{max.}$ (film) 3413 (OH) and 1721 cm^{-1}; δ 0·91br (6H, m), 1·16 (6H, s), 2·71 (1H, s), and 5·25 (1H, s) (Found: C, 72·5; H, 10·4. $C_{17}H_{28}O_3$ requires C, 72·8; H, 10·1%).

(+)-*Valerianol* [4βH,5α-*Eremophil*-1(10)-*en*-11-*ol*] (9).—The preceding acetate (0·5 g) in dry ether (30 ml) was added gradually (5 min) to a stirred solution of lithium metal (0·1 g) in liquid ammonia (100 ml), and the mixture was stirred for 20 min. Ammonium chloride (1·0 g) was then added and the ammonia was allowed to evaporate. The residue was treated with ice–water and the product was isolated by several extractions with ether. Evaporation of the combined, dried extracts yielded (+)-valerianol, accompanied by a diene hydrocarbon. The two were separated by preparative g.l.c. on a 15 ft column of 10% Carbowax 20M on Chromosorb G, at 200°, yielding (+)-valerianol (9) (0·35 g), the i.r. and n.m.r. spectra, and optical rotation of which were identical with those reported for the natural material.[15,16] The 3,5-dinitrobenzoate of the product separated from hexane in needles, m.p. 147·5°, alone or mixed with an authentic sample of (+)-valerianol 3,5-dinitrobenzoate, m.p. 147·5°.[15]

11,12-*Dihydronootkatone* [4βH,5α-*Eremophil*-1(10)-*en*-2-*one*] (16).—Crystalline (+)-nootkatone (1·02 g) in dry benzene (100 ml) was shaken in hydrogen at room temperature and pressure with chlorotristriphenylphosphinerhodium cata-

[24] G. Ohloff and W. Giersch, *Helv. Chim. Acta*, 1968, **51**, 1328.

lyst [25] (800 mg) for 1 h (uptake 1 mol. equiv.). The solution was allowed to percolate down a column of alumina (40 g) and eluted with benzene (6 × 25 ml). Evaporation of the solvent yielded 13,14-dihydronootkatone, which was distilled [b.p. 120° (bath) at 0·025 mmHg; yield 0·95 g], $\lambda_{max.}$ (EtOH) 238 nm (ε 15,000); $\nu_{max.}$ (film) 1681 and 1623 cm^{-1} (C=O and C=C) [no band at 890 (C=CH_2)]; δ 0·85—1·10 (12H, s and 2d overlapping) and 5·75 (1H, s) (Found: C, 81·7; H, 11·0. $C_{15}H_{24}O$ requires C, 81·8; H, 11·0%).

8,9-*Didehydro*-11,12-*dihydronootkatone* [4β*H*,5α-*Eremophila*-1(10),8-*dien*-2-*one*] (15).—The ketone (16) (0·66 g), *N*-bromosuccinimide (1·63 g, 3 mol), and dry carbon tetrachloride (30 ml) were refluxed on a water-bath in the dark for 5 h.[26] The mixture was cooled to 0°, and the solid material filtered off. The filtrate was concentrated *in vacuo*, leaving an orange, oily residue of the 9-bromo-ketone (17) (1·0 g). This was heated at 180° with freshly distilled γ-collidine (40 ml) for 45 min, then cooled and poured into an excess of ice-cold dilute hydrochloric acid. The *product*, isolated with ether, was distilled [b.p. 130° (bath) at 0·07 mmHg; yield 0·5 g]; $\lambda_{max.}$ (EtOH) 283 nm (ε 18,500); $\nu_{max.}$ (film) 1661 (C=O), 1623, 1590 (C=C), 1416 (CO·CH_2), and 1389 cm^{-1} (CMe_2); δ 0·95 (6H, d, *J* Hz), 1·00 (3H, d, *J* 9 Hz), 1·04 (3H, s), 2·00—2·20 (3H, m), 5·70 (1H, s), and 6·20 (2H, s); single spot on t.l.c. [development with petroleum (b.p. 30—60°)–ethyl acetate (4 : 1)] [Found: C, 82·3; H, 10·2%; *M* (mass spec.), 218. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%; *M*, 218]. The *semicarbazone*, separated from a small volume of methanol in cream-coloured elongated prisms, which were photochromic, m.p. 213° (decomp.), $\lambda_{max.}$ (EtOH) 297·5 nm (ε 24,100) (Found: C, 69·7; H, 9·3; N, 15·1. $C_{16}H_{25}N_3O$ requires C, 69·8; H, 9·2; N, 15·3%). The m.p. of this derivative was depressed (to 190—195°) on admixture with a sample of natural nardostachone semicarbazone [m.p. 232° (decomp.)].[18]

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[25] J. A. Osborn, F. H. Jardine, J. F. Young, and G. Wilkinson, *J. Chem. Soc.* (*A*), 1966, 1711; *cf.* ref. 20.

[26] *Cf.* K. Ziegler, A. Späth, E. Schaaf, W. Schumann, and E. Winkelmann, *Annalen*, 1942, **551**, 80.