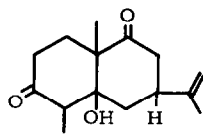
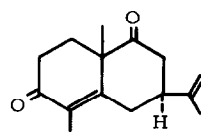


IV

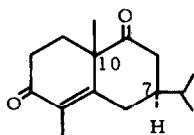


V

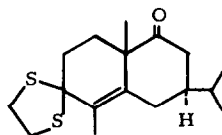


VI

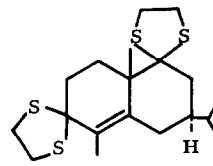
pyrrolidine gave V (m. p. 129-130°). Ketol V, when refluxed in benzene in the presence of pyrrolidine using a Dean-Stark water separator gave VI (85%; b. p. 142-148°/0.3 mm; m. p. 32°;  $\nu$  film 3085, 1711, 1670, 1645, 890  $\text{cm}^{-1}$ ;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  1.44(3H), 1.76(3H), 1.83(3H), 4.86(2H); mono-2,4-DNP m. p. 207-208°,  $\nu_{\text{nujol}}$  1710  $\text{cm}^{-1}$ ). Diketone VI could be prepared directly from IV in 76% yield by refluxing in benzene in the presence of pyrrolidine. Hydrogenation of VI in the presence of Pt/C gave VII (97%; m. p. 31-32°,  $\nu$  film 1710, 1670, 1385, 1375  $\text{cm}^{-1}$ ;



VII



VIII

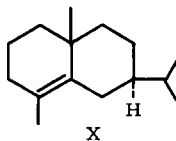


IX

$\delta_{\text{ppm}}^{\text{CCl}_4}$  0.97(6H, d,  $J=6\text{cps}$ ), 1.38(3H), 1.75(3H)). Diketone VII was also prepared from dihydro-IV via dihydro-V (m. p. 132°) or directly, as described above for the preparation of VI.

On treatment with an equimolar amount of ethanedithiol in the presence of p-toluenesulfonic acid, VII gave VIII (62%; m. p. 74.5-75°;  $\nu$  film 1703, 1620  $\text{cm}^{-1}$ ;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  0.94(6H, d,  $J=5.5\text{cps}$ ), 1.23(3H), 1.88(3H), 3.27(4H)) while in the presence of excess ethanedithiol, IX was obtained (70%; m. p. 107.5°;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  0.94(6H,  $J=5.5\text{cps}$ ), 1.25(3H), 1.86(3H), 3.20(8H)). The monothioacetal VIII was also further converted into IX with ethanedithiol.

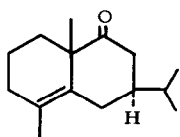
Desulfurization of IX with Raney nickel gave, after chromatography



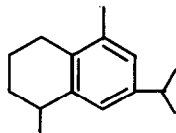
X

on silica gel impregnated with silver nitrate, racemic X (b. p. 90-95°/0.3 mm;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  0.92(6H, d,  $J=5.5$  cps), 0.98(3H), 1.56(3H)) identical in infrared and n. m. r. spectra and by g. l. c. with X of known absolute configuration obtained previously from the sesquiterpene neo-intermedeol.<sup>6</sup> This interconversion thus establishes the cis relationship at C-7 and C-10 in compounds VI-X. The stereospecific formation of VI and VIII, containing  $\beta$ -oriented C-7 substituents<sup>7</sup>, is of particular significance. McQuillin<sup>8</sup> first showed that condensation of dihydrocarvone with ethyl vinyl ketone yields, predominantly, ketols and  $\alpha, \beta$ -unsaturated ketones containing  $\alpha$ -oriented C-7 isopropenyl groups. A number of other workers have confirmed this observation.<sup>9</sup> However, on prolonged treatment with strong base, McQuillin reported that epimerization occurred via reverse Robinson annellation to give, in part, the thermodynamically more stable 7- $\beta$  epimer. Apparently, in the case of VI and VIII, the reverse reaction occurs readily even in the presence of a weak base, to give the stable anion of the 1,3-diketone, hydroxycarvone, and one obtains the thermodynamically more stable 7- $\beta$  isomer.<sup>10</sup> This is particularly advantageous because it opens the way to the ready synthesis of a number of eudesmane sesquiterpenes, all of which possess a cis C-7, C-10 relationship.

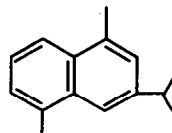
Desulfurization of VIII gave XI (b. p. 115-120°/0.2-0.3 mm;  $\nu^{\text{film}}$  1703, 1652  $\text{cm}^{-1}$ ;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  0.94 (6H, d,  $J=5.5$  cps), 1.18(3H), 1.64(3H);



XI



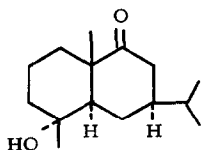
XII



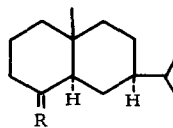
XIII

semicarbazone m. p. 197-200°). In the presence of  $\text{BF}_3$ -etherate in acetic acid XI gave XII (93%; b. p. 95-105°/0.2-0.4mm;  $\lambda$  cyclohexane 268(335), 276 $\mu$  (280);  $\nu$  film 1615, 1575  $\text{cm}^{-1}$ ;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  1.19(6H, d,  $J=6.5\text{cps}$ ), 2.06(3H), 6.78(1H), 6.86(1H).<sup>11</sup> Dehydrogenation of XII with Pd/C at 165-170° gave vetivalene<sup>12</sup>, XIII (81%;  $\lambda$  cyclohexane 278(5975), 288 $\mu$  (7170), rpt.<sup>13</sup> for 1,3,5-trimethylnaphthalene 277 (log  $\epsilon$  3.86), 2.89 $\mu$  (log  $\epsilon$  3.92);  $\delta_{\text{ppm}}^{\text{CCl}_4}$  1.35(6H, d,  $J=6.5\text{cps}$ ), 2.67(6H), 2.97(1H, multiplet); picrate m. p. 115.5-116.5°, rpt.<sup>12</sup> m. p. 115.5-116.5°). The previously reported<sup>3</sup> treatment of canarone with methyl magnesium iodide followed by dehydrogenation should have given XIII and not II assuming the correct structure of canarone is III. Unfortunately, we were unable to obtain a sample of this product or copies of its spectra for comparison with XIII. The previously synthesized II<sup>12</sup> is reported to give a picrate of different m. p. from that of the picrate of XIII.

Hydroboration of XI followed by oxidation with hydrogen peroxide and then sodium dichromate in acetic acid gave a mixture of ketols from which XIV (m. p. 93-95°;  $\nu$  film 3450, 1700  $\text{cm}^{-1}$ ;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  0.94 (6H, d,



XIV

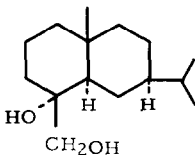
XV R=CH<sub>2</sub>

XVII R=O

$J=5.5\text{cps}$ ), 1.04(3H), 1.16(3H), 3.70(1H); semicarbazone m. p. 252-254°) was isolated after chromatography on silica gel. Dehydration of XIV with  $\text{POCl}_3$  in pyridine gave 7a(H)eudesm-4(14)en-9-one, III (93%; b. p. 98-105°/0.02-0.03mm;  $\nu$  film 3080, 1700, 1642, 885  $\text{cm}^{-1}$ ;  $\delta_{\text{ppm}}^{\text{CCl}_4}$  0.93(3H), 0.94(6H, d,  $J=5.5\text{cps}$ ), 4.60(1H), 4.82(1H); semicarbazone m. p. 191-192°). The infrared and n. m. r. spectra of III, thus obtained, were found to differ from the corresponding spectra of canarone, kindly supplied by Dr. S. C. Bhattacharyya. The n. m. r. spectrum of III was

much less complex in the region  $\delta$  1.0-3.0 than that of canarone, suggesting that canarone may be a mixture. In view of this discrepancy, further evidence was sought for the stereochemical assignment at C-5, C-7 and C-10 in III by correlation with eudesmol, a sesquiterpene of known stereochemistry.<sup>9a, 14</sup>

Huang-Minlon reduction of III gave XV (b. p. 90-93°/0.02mm;  $\nu$  film 3080, 1642, 885  $\text{cm}^{-1}$ ;  $\delta^{\text{CCl}_4}$  0.68(3H), 0.90(6H, d,  $J=5.5$  cps), 4.42(1H), 4.66(1H). Treatment of XV with osmium tetroxide gave diol XVI (m. p. 119.5-121°;  $\nu$  nujol 3380  $\text{cm}^{-1}$ ;  $\delta^{\text{CCl}_4}$  0.84(3H), 0.91(6H,



XVI

d,  $J=5.5$  cps), 2.57(2H), 3.65(2H, q,  $J=11, 14$  cps)). In the presence of lead tetraacetate diol XVI was converted into ketone XVII (b. p. 100-105°/0.3 mm;  $\nu$  film 1710, 1385, 1370  $\text{cm}^{-1}$ ;  $\delta^{\text{CCl}_4}$  0.73(3H), 0.92(6H, d,  $J=5.7$  cps); semicarbazone m. p. 212.5-213°) identical in infrared and n. m. r. spectra and by g. l. c. with XVII prepared from eudesmol acetate by ozonolysis, followed by pyrolysis to give  $\Delta^{11}$ -XVI and finally hydrogenation in the presence of Pt/C. Thus the stereochemistry of III is established at C-5 and further verified at C-7 and C-10.

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