

## MICROBIAL TRANSFORMATION OF SESQUITERPENOID—IV<sup>1</sup>

### PREPARATION OF 10-EPIGUAIOXIDE AND ITS IDENTIFICATION WITH BULNESOXIDE

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**Abstract**—*Streptomyces purpureus* has been found to oxidize guaioxide giving six monohydroxy-derivatives including 9 $\alpha$ -hydroxyguaioxide. Starting from the latter compound 10-epiguaioxide was prepared, this was found to be identical with bulnesoxide obtained by acid-catalysed cyclization of bulnesol. The structures of the other five hydroxylation products are described.

WE PREVIOUSLY determined the structure of guaioxide<sup>2</sup> and liguloxide (4-epiguaioxide)<sup>3</sup> using microbial hydroxylation of the former compound.

Meanwhile Chiurdoglu *et al.*,<sup>4</sup> found that sulphuric acid treatment of bulnesol (I) in an acetic acid solution gave a 5:4 mixture of two cyclization products, guaioxide and bulnesoxide, although the total yield was poor (4.7%). Considering that guaioxide was already known to be obtainable by similar treatment of guaiol (II),<sup>5</sup> and taking the view that *trans* addition of the OH group to the double bond must have occurred, they suggested the structures III and IV for bulnesoxide and guaioxide, respectively.<sup>4</sup> Later the structure of guaioxide was established as V.<sup>2, 6, 7</sup>

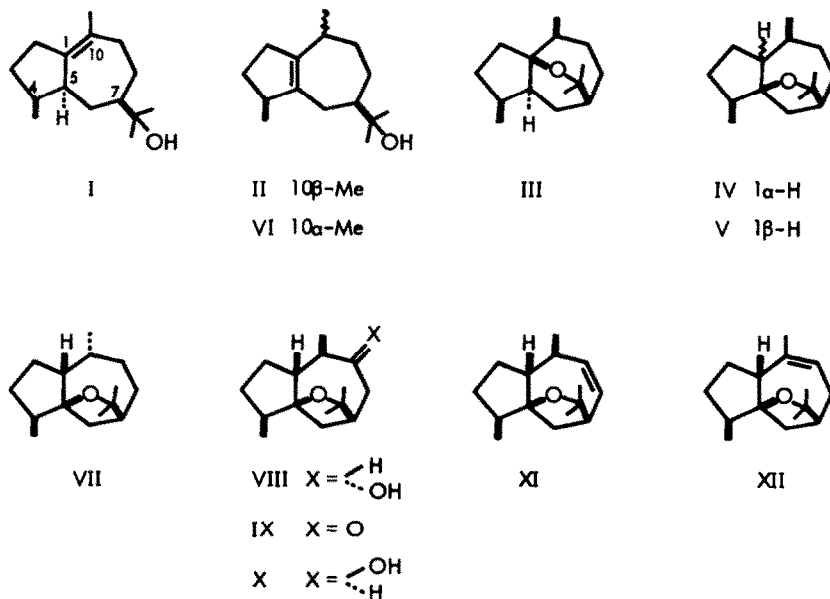


CHART 1

On the other hand, Bates and Slagel<sup>8</sup> reported that similar acid treatment of bulnesol (I) for a shorter time resulted in the double bond migration giving rise to a 1 : 1 mixture of gualiol (II) and 10-epigualiol (VI) in a total yield of 18%. Taking into account these two experimental results,<sup>4,8</sup> we considered that bulnesoxide might be produced by acid-catalysed cyclization of the OH group in 10-epigualiol to the C-5 position as in the formation of guaiooxide,<sup>2,6</sup> i.e. bulnesoxide might have the structure 10-epiguaiooxide (VII).

In the course of our search for microorganisms capable of oxidizing guaiooxide,<sup>2</sup> we found that *Streptomyces purpurescens* oxidized this substrate to give several monohydroxy-derivatives and that one of them was 9 $\alpha$ -hydroxyguaiooxide (VIII), a compound useful for preparing 10-epiguaiooxide. This afforded a good opportunity for confirming the above assumption.

The product VIII, C<sub>15</sub>H<sub>26</sub>O<sub>2</sub>, m.p. 118–121°, showed an IR band at 3625 cm<sup>-1</sup> (OH), and on Jones oxidation gave a ketone (IX). Reduction of IX with sodium in EtOH afforded the original alcohol (VIII), indicating that the ketone (IX) retains the same stereochemistry as VIII. The ketone (IX) showed an IR band at 1703 cm<sup>-1</sup> (seven-membered ring ketone), indicating that the carbonyl group in IX is present at C-8 or C-9. Since IX is not identical with 8-oxoguaiooxide derived from the known 8 $\alpha$ -hydroxyguaiooxide,<sup>2</sup> it must be 9-oxoguaiooxide. LAH reduction of IX gave predominantly an epimeric alcohol (X). The IR spectrum of a dilute solution of X in CCl<sub>4</sub> showed

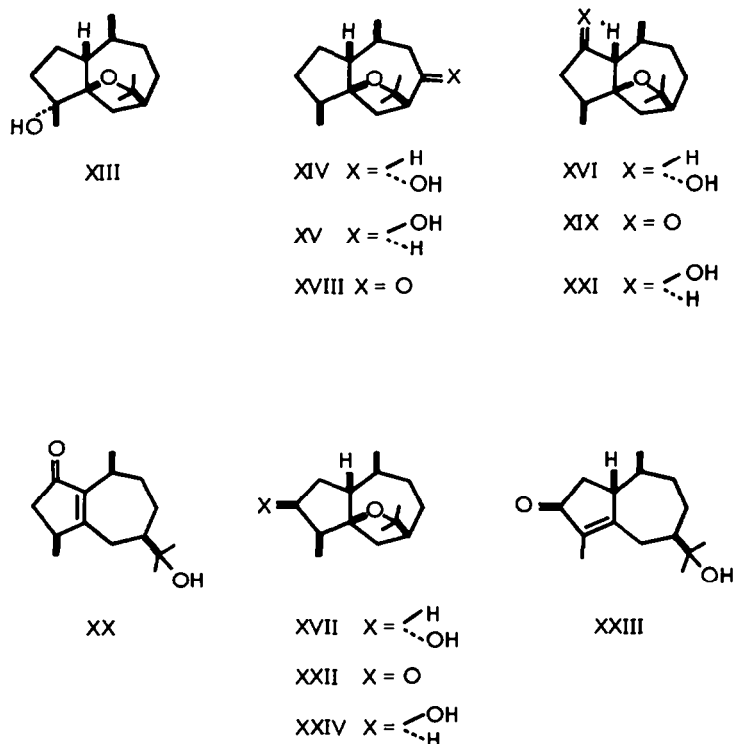


CHART 2

evidence for an intramolecular hydrogen bond ( $\nu_{\max}$  3420  $\text{cm}^{-1}$ ) between the OH group at C-9 and 5 $\beta$ -ethereal oxygen atom, indicating that X has a 9 $\beta$ -OH group and thus that the product VIII is 9 $\alpha$ -hydroxyguaiooxide.

9 $\beta$ -Hydroxyguaiooxide (X) when heated with TsCl in pyridine yielded a 2:3 mixture of two dehydrated products (XI and XII). Since XI was identical with the known 8-dehydroguaiooxide ( $\delta$  5.43, 2H),<sup>2</sup> the other product XII had to be the 9-dehydro compound ( $\delta$  1.67, 3H, and 5.17, 1H). Catalytic hydrogenation of XII gave a 3:2 mixture of guaiooxide (V) and its 10-epimer (VII), separated by prep. GLC.

The IR spectrum of 10-epiguaiooxide (VII) is very similar to that of bulnesoxide,<sup>4</sup> but the latter shows two weak extra bands at 1250 and 1090  $\text{cm}^{-1}$ ; the NMR spectrum of bulnesoxide<sup>4</sup> also shows a few additional signals to that of 10-epiguaiooxide. From these facts, we considered that the bulnesoxide<sup>4</sup> must contain a small amount of the by-product. However, attempts to detect the by-product on GLC under various conditions were unsuccessful.

We found that treatment of bulnesol (I) with  $\text{HClO}_4$ <sup>9</sup> in place of  $\text{H}_2\text{SO}_4$  in an AcOH medium gave a crystalline oxide,  $\text{C}_{15}\text{H}_{26}\text{O}$ , m.p. 27°, of the same retention time as bulnesoxide,<sup>4</sup> together with guaiooxide. Injection of the crystalline material into the oily bulnesoxide prepared by Chiurdoglu's procedure led to crystallization of the major part of the latter. Thus the oxide of m.p. 27° proved to be pure bulnesoxide. The IR, NMR and mass spectra of the crystalline oxide were superimposable with those of 10-epiguaiooxide derived from 9 $\alpha$ -hydroxyguaiooxide. The structure of bulnesoxide is therefore confirmed as VII.

In our fermentation experiment, we isolated another five hydroxylation products (XIII–XVII). Two of them (XIII and XIV) were the known 4 $\alpha$ -hydroxy-<sup>2</sup> and 8 $\alpha$ -hydroxyguaiooxide,<sup>2</sup> respectively.

The fourth product (XV),  $\text{C}_{15}\text{H}_{26}\text{O}_2$ , m.p. 122–123°,  $\nu_{\max}$  3585  $\text{cm}^{-1}$  (OH), on Jones oxidation afforded a ketone (XVIII), identical with the ketone obtained by similar oxidation of XIV. Thus the product XV is 8 $\beta$ -hydroxyguaiooxide.

The fifth product (XVI),  $\text{C}_{15}\text{H}_{26}\text{O}_2$ , m.p. 96–97°,  $\nu_{\max}$  3610  $\text{cm}^{-1}$  (OH), was oxidized with Jones reagent to give a ketone (XIX),  $\nu_{\max}$  1733  $\text{cm}^{-1}$  (five-membered ring ketone), not identical with 6-oxoguaiooxide.<sup>1</sup> Hence the carbonyl group in XIX must be located at C-2 or C-3. When passed through a column of alumina the ketone (XIX) underwent opening of its ether linkage to give an  $\alpha\beta$ -unsaturated ketone (XX),  $\nu_{\max}$  1690 and 1639  $\text{cm}^{-1}$ . The NMR spectrum of XX shows two doublet Me signals ( $\delta$  0.99, 3H, and 1.13, 3H), indicating that XX is a  $\Delta^{1,5}$ -2-oxo compound, i.e. the product XVI has the OH group at C-2. LAH reduction of XIX gave a 1:4 mixture of XVI and its epimeric alcohol (XXI). Benzoates were prepared from both alcohols XVI and XXI, and their  $\Delta[\text{M}]_D$  values were compared.<sup>10</sup> For the product XVI series the  $\Delta[\text{M}]_D$  value was +114°, whereas for the epimer XXI series the value was –80°. Thus the product XVI has the 2S-configuration (2 $\alpha$ -OH) and its epimer XXI, the 2R-configuration (2 $\beta$ -OH).

The last product (XVII),  $\text{C}_{15}\text{H}_{26}\text{O}_2$ , m.p. 50–52°, also gave a five-membered ring ketone (XXII),  $\nu_{\max}$  1738  $\text{cm}^{-1}$ , on Jones oxidation. Treatment of XXII with alumina afforded an  $\alpha\beta$ -unsaturated ketone (XXIII) identical with 8-deoxytorilolone,<sup>2</sup> showing that the OH group in XVII is present at C-3. LAH reduction of XXII gave a 1:1 mixture of epimeric alcohols XVII and XXIV. Configuration of the OH group in both compounds was also determined by application of benzoate rule.<sup>10</sup> The  $\Delta[\text{M}]_D$  value for the XVII series was –104° and that for the XXIV series was +242°. Thus the product

XVII has the 3R-configuration (3 $\alpha$ -OH) and the epimer XXIV, the 3S-configuration (3 $\beta$ -OH).

### EXPERIMENTAL

Optical rotations were taken in dioxane unless otherwise stated. NMR spectra were recorded on a Varian A-60 spectrometer in CDCl<sub>3</sub> with TMS as internal standard. GLC was run using an Aerograph Autoprep A-700 instrument.

*Fermentation of guaioixide (V) with Streptomyces purpureus.* Forty 500 ml shaking flasks, each containing 100 ml of sterilized "Bennet medium" composed of 1% glucose, 0.2% "Bact" yeast extract, 0.1% Ehrlich beef extract and 0.2% "N-Z-Amine Type A" (pH of the medium was adjusted by 10% NaOH aq to 7.0), were inoculated with *Streptomyces purpureus*. After shaking at 27° for 2 days, a soln of guaioixide (33 mg) in MeOH (0.3 ml) was added to each flask and the fermentation continued at 27° for a further 5 days. The filtrate of the culture broths was extracted with CHCl<sub>3</sub>-MeOH (3:2) and the extract evaporated leaving a brown oil (1.663 g).

The oil was chromatographed on silica gel (50 g) and eluted successively with light petroleum and light petroleum-ether (9:1, 4:1 and 1:1) to give 16 fractions. Combination of the fractions having identical or similar TLC properties gave 6 larger fractions. Fr. 2 (240 mg) was distilled at 80° (bath)/5 mm to recover guaioixide (V) as an oil (230 mg) (IR spectrum and retention time).

*2 $\alpha$ -Hydroxyguaioixide (XVI).* Fr. 4 (319 mg) was subjected to a second chromatography on silica gel (15 g) and eluted with light petroleum-ether (9:1, 85:15 and 4:1). The eluate with the 85:15 mixture (194 mg) was acetylated with Ac<sub>2</sub>O (0.5 ml) and pyridine (0.5 ml) overnight at room temp. The usual work up gave an oil (210 mg), separated by chromatography on silica gel (20 g) into 2 $\alpha$ -acetoxyguaioixide [eluted with light petroleum-ether (9:1)], an oil (120 mg),  $[\alpha]_D^{26} + 8.0^\circ (\pm 0.7^\circ)$  (c 0.678),  $\nu_{\max}$  (film) 1735, 1250 and 1240 cm<sup>-1</sup> (OAc), and 4 $\alpha$ -hydroxyguaioixide (XIII)<sup>2</sup> [eluted with light petroleum-ether (4:1)], an oil (29 mg) (IR spectrum and retention time).

*2 $\alpha$ -Acetoxyguaioixide (120 mg)* was dissolved in 5% KOH-MeOH (5 ml) and the soln refluxed under N<sub>2</sub> atm. for 1 hr. Working up in the usual manner gave 2 $\alpha$ -hydroxyguaioixide (XVI) as plates (89 mg), m.p. 96-97° (sublimation),  $[\alpha]_D^{25} - 21.7^\circ (\pm 0.8^\circ)$  (c 0.748),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3610 and 3450 cm<sup>-1</sup> (OH),  $\delta$  0.98 (3H, d,  $J = 5$  Hz) and 0.99 (3H, d,  $J = 7$  Hz) (4-Me and 10-Me), 1.17 (3H, s) and 1.45 (3H, s) (11-Me<sub>2</sub>), and 4.19 (1H, m, 2-H). (Found: C, 75.6; H, 11.2. C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> requires: C, 75.6; H, 11.0%). The benzoate had m.p. 87-89°,  $[\alpha]_D^{22} + 18.3^\circ (\pm 0.6^\circ)$  (c 0.951). (Found: C, 77.15; H, 8.75. C<sub>22</sub>H<sub>30</sub>O<sub>3</sub> requires: C, 77.15; H, 8.85%).

*8 $\beta$ -Hydroxyguaioixide (XV).* The eluate (52 mg) with light petroleum-ether (4:1) from the second chromatography (see above) was acetylated as before. The mixture (60 mg) was divided into five fractions by prep. TLC [silica gel; C<sub>6</sub>H<sub>6</sub>-EtOAc (9:1); Morin-UV]. The fraction having the third highest mobility gave 8 $\alpha$ -acetoxyguaioixide<sup>2</sup> as prisms (20 mg), m.p. 56-57° (sublimation) (m.m.p. and IR).

The fourth TLC fraction gave an oil (13 mg), hydrolysed with 5% KOH-MeOH as above to give 8 $\beta$ -hydroxyguaioixide (XV) prisms (9 mg), m.p. 122-123° (sublimation),  $[\alpha]_D^{24} - 1.2^\circ (\pm 0.5^\circ)$  (c 0.859),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3585 cm<sup>-1</sup> (OH),  $\delta$  0.95 (3H, d,  $J = 6$  Hz) and 0.98 (3H, d,  $J = 6$  Hz) (4-Me and 10-Me), 1.19 (3H, s) and 1.50 (3H, s) (11-Me<sub>2</sub>), and 3.77 (1H, broad m, 8-H). (Found: C, 75.35; H, 11.15. C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> requires: C, 75.6; H, 11.0%). Jones oxidation of XV gave 8-oxoguaioixide (XVIII), an oil,  $[\alpha]_D^{23} + 86.7^\circ (\pm 2.4^\circ)$  (c 0.534),  $\nu_{\max}$  (film) 1693 cm<sup>-1</sup> (cyclopentanone),  $\delta$  0.98 (3H, d,  $J = 6$  Hz, 4-Me), 1.05 (3H, d,  $J = 6.5$  Hz, 10-Me), and 1.23 (3H, s) and 1.28 (3H, s) (11-Me<sub>2</sub>). (Found: C, 75.95; H, 10.15. C<sub>15</sub>H<sub>24</sub>O<sub>2</sub> requires: C, 76.2; H, 10.25%), identical with an authentic sample prepared similarly from 8 $\alpha$ -hydroxyguaioixide<sup>2</sup> (IR and retention time).

*3 $\alpha$ -Hydroxyguaioixide (XVII).* Fr. 5 (135 mg) showed two peaks of retention times 9.3 min (60%) and 11.5 min (40%) on GLC (5% QF-1; 160°; He 100 ml/min). The compound of retention time 9.3 min was 3 $\alpha$ -hydroxyguaioixide (XVII), prisms, m.p. 50-52° (sublimation),  $[\alpha]_D^{22} - 49.6^\circ (\pm 1.1^\circ)$  (c 0.780),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3605 and 3440 cm<sup>-1</sup> (OH)  $\delta$  0.91 (3H, diffuse d, 10-Me), 1.03 (3H, d,  $J = 7$  Hz, 4-Me), 1.15 (3H, s) and 1.30 (3H, s) (11-Me<sub>2</sub>), and 3.70 (1H, m, 3-H). (Found: C, 75.4; H, 10.9. C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> requires: C, 75.6; H, 11.0%). The benzoate was an oil,  $[\alpha]_D^{23} - 65.0^\circ (\pm 2.7^\circ)$  (c 0.383). (Found: C, 77.0; H, 8.65. C<sub>22</sub>H<sub>30</sub>O<sub>3</sub> requires: C, 77.15; H, 8.85%).

*9 $\alpha$ -Hydroxyguaioixide (VIII).* The compound of retention time 11.5 min on the above GLC was 9 $\alpha$ -hydroxyguaioixide (VIII), prisms, m.p. 118-121° (sublimation),  $[\alpha]_D^{23} - 32.4^\circ (+ 0.8^\circ)$  (c 0.861),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3625 and 3450 cm<sup>-1</sup> (OH),  $\delta$  0.97 (3H, d,  $J = 6$  Hz, 4-Me), 1.02 (3H, d,  $J = 6$  Hz, 10-Me), 1.15

(3H, s) and 1.32 (3H, s) (11-Me<sub>2</sub>), and 3.83 (1H, m, 9-H). (Found: C, 75.55; H, 11.25. C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> requires: C, 75.6; H, 11.0%).

**9-Oxoguaioxide (IX).** Jones oxidation of VIII in the usual manner gave 9-oxoguaioxide (IX) prisms, m.p. 52–55° (sublimation),  $[\alpha]_D^{25} - 8.6^\circ (\pm 0.5^\circ)$  (c 1.011),  $\nu_{\max}$  (CHCl<sub>3</sub>) 1703 cm<sup>-1</sup> (cyclopentanone),  $\delta$  0.97 (3H, d,  $J = 7$  Hz, 4-Me), 1.03 (3H, d,  $J = 6$  Hz, 10-Me), and 1.17 (3H, s) and 1.27 (3H, s) (11-Me<sub>2</sub>). (Found: C, 76.5; H, 10.2. C<sub>15</sub>H<sub>24</sub>O<sub>2</sub> requires: C, 76.2; H, 10.25%).

**Reduction of 9-oxoguaioxide (IX) with sodium in EtOH.** To a soln of IX (60 mg) in abs EtOH (3 ml), sodium (200 mg) was added portionwise and the mixture heated under reflux for 5 hr. Water was added and the mixture extracted with CHCl<sub>3</sub>, washed, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated leaving a crystalline substance (60 mg). This was chromatographed on silica gel (10 g). Elution with light petroleum–ether (9:1) gave 4 mg of 9 $\beta$ -hydroxyguaioxide (X) (see below). Further elution with light petroleum–ether (4:1) afforded starting material (18 mg) (IR spectrum). Final elution with light petroleum–ether (1:1) yielded 9 $\alpha$ -hydroxyguaioxide (VIII) (31 mg) (m.m.p. and IR).

**9 $\beta$ -Hydroxyguaioxide (X).** A soln of IX (50 mg) in dry ether (2 ml) was added dropwise to a suspension of LAH (50 mg) in dry ether (3 ml) and the mixture stirred at room temp. for 1 hr. Excess reagent was decomposed by addition of water and the mixture extracted with CHCl<sub>3</sub>, washed, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated to give a pale yellow oil (49 mg), purified by chromatography on silica gel to yield 9 $\beta$ -hydroxyguaioxide (X) as prisms (42 mg), m.p. 53–54° (sublimation),  $[\alpha]_D^{22} + 9.3^\circ (\pm 0.5^\circ)$  (c 0.969),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3420 cm<sup>-1</sup> (OH),  $\delta$  0.98 (3H, d,  $J = 6$  Hz, 4-Me), 1.05 (3H, d,  $J = 6$  Hz, 10-Me), 1.20 (3H, s) and 1.48 (3H, s) (11-Me<sub>2</sub>), and 3.63 (1H, m, 9-H). (Found: C, 75.9; H, 10.95. C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> requires: C, 75.6; H, 11.0%).

**Conversion of 9 $\beta$ -hydroxyguaioxide (X) into guaioxide (V) and 10-epiguaioxide (VII).** TsCl (500 mg) was added portionwise to a soln of X (220 mg) in pyridine (6 ml) and the mixture heated at 100° for 5 hr. The mixture was poured into ice–water and extracted with CHCl<sub>3</sub>, purified by chromatography on silica gel (20 g) giving a pale yellow oil (133 mg), separated into two fractions by prep. TLC (silica gel; C<sub>6</sub>H<sub>6</sub>; Morin—UV). The upper fraction gave 9-dehydroguaioxide (XII), an oil (67 mg),  $\delta$  1.01 (3H, d,  $J = 7$  Hz, 4-Me), 1.17 (3H, s) and 1.23 (3H, s) (11-Me<sub>2</sub>), 1.67 (3H, d,  $J = 1.7$  Hz, 10-Me), and 5.17 (1H, m, 9-H). The lower fraction gave 8-dehydroguaioxide (XI) an oil (58 mg), identical with an authentic sample<sup>2</sup> (IR and retention time).

A mixture of XII (67 mg) and Adams' catalyst (30 mg) in AcOH (6 ml) was hydrogenated at room temp. When 1.1 mole H<sub>2</sub> had been absorbed, the reaction stopped, and the catalyst and solvent were removed. The residue (65 mg) showed two peaks of retention times 17.5 min (60%) and 21.1 min (40%) on GLC (5% DEGS; 100°; He 100 ml/min). The compound of retention time 17.5 min was guaioxide (V) (IR and retention time). The compound of retention time 21.1 min was 10-epiguaioxide (VII), an oil,  $[\alpha]_D^{25} - 9.3^\circ (\pm 0.8^\circ)$  (c 0.593 CHCl<sub>3</sub>),  $\delta$  0.95 (3H, d,  $J = 6$  Hz) and 0.98 (3H, d,  $J = 6.5$  Hz) (4-Me and 10-Me), and 1.18 (3H, s) and 1.36 (3H, s) (11-Me<sub>2</sub>). (Found: C, 80.95; H, 11.85. C<sub>15</sub>H<sub>26</sub>O requires: C, 81.0; H, 11.8%).

**Treatment of bulnesol (I) with HClO<sub>4</sub> in AcOH.** To a soln of I (4 g) in 98% AcOH (50 ml), 20% HClO<sub>4</sub> aq (0.6 ml) was added, and the mixture set aside at room temp for 40 hr. The mixture was diluted with water, extracted with ether, washed free from acid and dried (Na<sub>2</sub>SO<sub>4</sub>). Removal of solvent gave a pale brown oil (4.0 g), chromatographed on silica gel (60 g) and eluted with light petroleum and light petroleum–ether (99:1, 98:2 and 4:1). The fraction eluted with light petroleum–ether (98:2) (490 mg) was treated with LAH (100 mg)<sup>4</sup> to convert the acetylated product into the OH compound. The product (450 mg) thus obtained was chromatographed on silica gel (20 g) to remove the OH compound (203 mg). Elution with light petroleum–ether (98:2) gave an oil (245 mg), which showed two peaks of retention times 17.5 min (55%) and 21.1 min (45%) on GLC (5% DEGS; 100°; He ml/min). The compound of retention time 17.5 min was guaioxide (V) (IR spectrum and retention time). The compound of retention time 21.1 min was bulnesoxide (VII), plates, m.p. 27° (sublimation),  $[\alpha]_D^{25} - 8.2^\circ (\pm 0.6^\circ)$  (c 0.797 CHCl<sub>3</sub>). (Found: C, 81.15; H, 11.85. C<sub>15</sub>H<sub>26</sub>O requires: C, 81.0; H, 11.8%), identical with an authentic sample of 10-epiguaioxide (see above) (IR, NMR and mass spectra, and retention time).

**2-Oxoguaioxide (XIX).** Jones oxidation of 2 $\alpha$ -hydroxyguaioxide (XVI) as above gave the ketone (XIX) as prisms, m.p. 80–81° (sublimation),  $[\alpha]_D^{25} - 200.7^\circ (\pm 2.6^\circ)$  (c 0.920),  $\nu_{\max}$  (CHCl<sub>3</sub>) 1733 cm<sup>-1</sup> (cyclopentanone),  $\delta$  (C<sub>6</sub>D<sub>6</sub>) 1.03 (3H, d,  $J = 7$  Hz, 4-Me), 1.02 (3H, s) and 1.18 (3H, s) (11-Me<sub>2</sub>), and 1.31 (3H, d,  $J = 5$  Hz, 10-Me), ORD  $[\phi]_{400} - 2533^\circ$ ,  $[\phi]_{327} - 17,286^\circ$ ,  $[\phi]_{282} + 14,271^\circ$ ,  $[\phi]_{237} + 7457^\circ$  (c 0.920, t = 25°). (Found: C, 76.55; H, 10.3. C<sub>15</sub>H<sub>24</sub>O<sub>2</sub> requires: C, 76.2; H, 10.25%).

**Rearrangement of 2-oxoguaioxide (XIX) on alumina.** A soln of XIX (70 mg) in light petroleum (2 ml)

was placed on a column of alumina (20 g, activity V) and left overnight. Elution with ether gave the product (XX), a viscous oil (66 mg),  $[\alpha]_D^{25} - 70.4^\circ (\pm 2.8^\circ)$  (*c* 0.935),  $\lambda_{\max}$  (EtOH) 241.5  $\mu$  ( $\epsilon$  13,600),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3600 (OH), 1690 and 1639  $\text{cm}^{-1}$  (cyclopentenone),  $\delta$  0.99 (3H, d,  $J = 7$  Hz, 4-Me), 1.13 (3H, d,  $J = 7$  Hz, 10-Me), and 1.22 (3H, s) and 1.27 (3H, s) (11-Me<sub>2</sub>). (Found: C, 76.1; H, 10.4. C<sub>15</sub>H<sub>24</sub>O<sub>2</sub> requires: C, 76.2; H, 10.25%).

2 $\beta$ -Hydroxyguaioixide (XXI). A soln of XIX (255 mg) in dry ether (5 ml) was reduced with LAH (120 mg) in dry ether (5 ml) as above to give a crystalline product (230 mg), which was divided into two fractions by prep. TLC [silical gel; C<sub>6</sub>H<sub>6</sub>-EtOAc (4 : 1); Morin—UV]. The upper fraction gave 2 $\alpha$ -hydroxyguaioixide (XII) as plates (44 mg), m.p. 96–97° (sublimation) (m.m.p. and IR). The lower fraction yielded 2 $\beta$ -hydroxyguaioixide (XXI) prisms (174 mg), m.p. 107–108° (sublimation),  $[\alpha]_D^{25} - 70.7^\circ (\pm 1.3^\circ)$  (*c* 0.861),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3610 and 3475  $\text{cm}^{-1}$  (OH),  $\delta$  1.13 (6H, d,  $J = 7$  Hz, 4-Me and 10-Me), 1.14 (3H, s) and 1.30 (3H, s) (11-Me<sub>2</sub>), and 3.68 (1H, m, 2-H). (Found: C, 75.7; H, 11.0. C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> requires: C, 75.6; H, 11.0%). The benzoate had m.p. 65–67°.  $[\alpha]_D^{22} - 72.6^\circ (\pm 1.1^\circ)$  (*c* 1.060). (Found: C, 77.5; H, 8.85. C<sub>22</sub>H<sub>30</sub>O<sub>3</sub> requires: C, 77.15; H, 8.85%).

3-Oxoguaioixide (XXII). Compound XVII was oxidized with Jones reagent as before to give 3-oxoguaioixide (XXII) as an oil,  $[\alpha]_D^{22} + 116.1^\circ (\pm 6.4^\circ)$  (*c* 0.242),  $\nu_{\max}$  (CHCl<sub>3</sub>) 1738  $\text{cm}^{-1}$  (cyclopentanone),  $\delta$  0.95 (3H, d,  $J = 6$  Hz, 10-Me), 1.13 (3H, d,  $J = 7$  Hz, 4-Me), and 1.16 (3H, s) and 1.33 (3H, s) (11-Me<sub>2</sub>), ORD  $[\phi]_{400} + 952^\circ$ ,  $[\phi]_{326.5} + 10,109^\circ$ ,  $[\phi]_{281} - 9947^\circ$ ,  $[\phi]_{240} - 5714^\circ$  (*c* 0.242,  $t = 22^\circ$ ). (Found: C, 76.1; H, 10.15. C<sub>15</sub>H<sub>24</sub>O<sub>2</sub> requires: C, 76.2; H, 10.25%).

Rearrangement of 3-oxoguaioixide (XXII) on alumina. Compound XXII (62 mg) was treated on a column of alumina as above to give the product (XXIII), prisms (55 mg), m.p. 70–71° (sublimation), identical with an authentic sample of 8-deoxytolilolone<sup>2</sup> (m.m.p. and IR).

3 $\beta$ -Hydroxyguaioixide (XXIV). The ketone XXII (100 mg) was reduced with LAH (100 mg) as above to give the product (94 mg), which showed two peaks of retention times 9.3 min (50%) and 11.5 min (50%) on GLC (5% QF-1; 160°; He 100 ml/min). The compound of retention time 9.3 min was 3 $\alpha$ -hydroxyguaioixide (XVII), m.p. 50–52° (m.m.p. and IR). The compound of retention time 11.5 min was 3 $\beta$ -hydroxyguaioixide (XXIV), prisms, m.p. 90–91° (sublimation),  $[\alpha]_D^{22} - 112.9^\circ (\pm 2.0^\circ)$  (*c* 0.750),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3605 and 3430  $\text{cm}^{-1}$  (OH),  $\delta$  0.89 (3H, d,  $J = 4.5$  Hz, 10-Me), 0.99 (3H, d,  $J = 7$  Hz, 4-Me), 1.15 (3H, s) and 1.30 (3H, s) (11-Me<sub>2</sub>), and 4.03 (1H, m, 3-H). (Found: C, 75.65; H, 11.1. C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> requires: C, 75.6; H, 11.0%). The benzoate was an amorphous solid, m.p. 47–56°,  $[\alpha]_D^{23} - 8.0^\circ (\pm 0.9^\circ)$  (*c* 0.816). (Found: C, 76.9; H, 8.7. C<sub>22</sub>H<sub>30</sub>O<sub>3</sub> requires: C, 77.15; H, 8.85%).

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