samples. UV–visible spectra were recorded on a Cary 17 spectrometer. Gas chromatography/mass spectrometry was performed on a Hewlett-Packard 5980A instrument using an OVM-1 column. Some difficulty was encountered in the GC/MS experiments because 1 decomposes in the instrument. Best results were obtained with the injector at 100 °C and temperature programming from 40 to 130 °C at 8 °C/min. Mass spectra were recorded on both the reaction of 1 and 2 as well as for 1 alone. The reaction mixture gave four peaks in addition to those observed for 1 alone. Two of these components are isobutene (5) and unreacted methyl trifluoromethanesulfonate (2); the other two components are unidentified but gave their largest mass peaks at m/e 72 and 89, respectively.

Compounds. Di-*tert*-butyl nitroxide (1) and methyl trifluoromethanesulfonate (2) were commercial compounds and used as received. 2-Methyl-2-nitrosopropane (6) and CF_3SO_3D were synthesized as shown below.

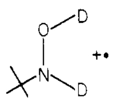
2-Methyl-2-nitrosopropane (6). Compound 6 was prepared by a modification of the method of Stowell.[12] A solution of *tert*-butylamine (1 mol) and sodium tungstate ($Na_2WO_4\cdot 2H_2O$, 8 g) in 100 mL of water was cooled in an ice/brine bath. Hydrogen peroxide solution (206 mL of 30% H_2O_2 plus 100 mL of H_2O) was added dropwise with stirring at a rate that maintained the temperature below 25 °C. A blue-green layer was seen to form on top of the aqueous layer. After the addition of all the peroxide, the literature procedure was modified slightly. Attempts to work up the reaction by Stowell's method led to large mechanical losses as the blue monomer dimerized, coating the apparatus with a white solid. To avoid this, we extracted the reaction mixture with several portions of 100–115 °C ligroine. Distillation of the combined extracts gave a brilliant blue liquid (bp 50 °C) which turned to white needles upon cooling. Care must be taken that the dimerization product (the needles) does not clog the distillation apparatus. The modified procedure gave a slightly better yield (26%) than reported by Stowell.

The compound gave a UV–vis value for λ_{max} of 677 nm. This band was used to characterize 6 which is produced in the reaction of 1 and 2.

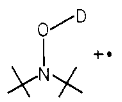
Trifluoromethanesulfonic Acid-*d*. (a) Trifluoromethanesulfonic anhydride (triflic anhydride) was prepared by dehydration of triflic acid. A 100-mL flask was charged with fresh, anhydrous P_2O_5 (25 g) and triflic acid (20 mL) and stirred for 1 h. The flask was then equipped for distillation over a short Vigreux column, and 11–12 mL (ca. 19 g) of anhydride was distilled; bp 82–83.5 °C [lit. bp 81–83 °C (745 mm)]. The anhydride was sealed in glass ampules under Ar until needed.

(b) CF_3SO_3D was produced by reaction of triflic anhydride with D_2O. Triflic anhydride (11 mL, 0.03 mol) and D_2O (0.59 g, 0.03 mol) were placed in a heavy-walled Pyrex tube which was cooled and sealed. The tube was placed in a 100 °C oil bath overnight, or until two phases were no longer visible. The tube was cooled and opened, and the contents were distilled; bp 164–164.7 °C. Mass spectrometry showed the product to be free of D_2O, H_2O, and the protic acid.

Reaction of 1 with CF_3SO_3D/2. ESR Study. If 9 is the correct structure for the new paramagnetic species produced in the reaction of 1 with CF_3SO_3D, the ESR spectrum of the corresponding species (I) produced in CF_3SO_3D will lie under the spectrum of II.[13] If, on the other hand, the paramagnetic species had $a_N = 21$ G, $a_N = 14$ G, and $a_H = 3$ G, many of the lines for the corresponding deuterated species would not lie under those for II. Although not well resolved, only three broad signals were observed. Lines attributable to the latter paramagnetic species, resolved or not, would have been easily detected outside the domain of the three broad signals; these lines were not observed.[14] Thus, 9 is consistent with the ESR spectrum and the other species is not.



I



II

Acknowledgment. R.J.S. thanks the Gulf Oil Co. for fellowship support.

Registry No. 1, 2406-25-9; 2, 333-27-7; 6, 917-95-3; 8, 78698-38-1; 9, 78698-39-2.

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[12] Stowell, J. C. *J. Org. Chem.* 1971, *36*, 3055.

[13] For a discussion of how one can calculate the ESR spectrum of a deuterated species if the ESR spectrum of the protio species is known, see: Wertz, J. E.; Bolton, J. R. "Electron Spin Resonance"; McGraw-Hill: New York, 1972.

[14] For a detailed discussion and analysis of these points see: Smith, R. J.; Ph.D. Dissertation, University of Tennessee, 1980.

On Some Guaiol Oxidation Products[1]

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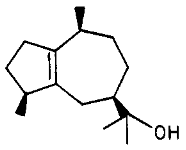
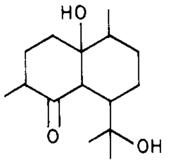


I



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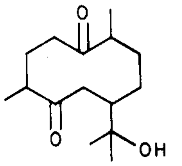
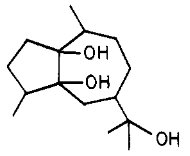


III



IV

Oxidation of the sesquiterpene alcohol guaiol (I) with potassium permanganate was first described by Semmler and Mayer in 1912.[4] Nearly 30 years later, Ruzicka and Haagen-Smit reinvestigated this reaction[5] and determined the correct composition of the high-melting (220 °C) reaction product. Furthermore, they demonstrated that it was also formed on ozonolysis of guaiol.[5] Its structure, as the ketol II, was finally deduced by Plattner and Magyar inter alia by conversion to cadalene.[6] These workers suggested that diketone III was an intermediate in the formation of II, and thus oxidative degradation of guaiol became an important part in the proof its structure. More recently, Takeda and Minato obtained triol IV from I and oxidatively transformed it to II.[7] Also, Nadgouda et al. have reported[8] the conversion of diketone III to ketol II under basic conditions. Thus the reaction sequence I → IV → III → II apears justified.

Our interest in these reactions had two initial objectives: (i) to develop a preparative method for obtaining ketol II and if possible diketone III and (ii) to determine the stereochemistry of the guaiol oxidation products. In this

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[1] Portions of this work were presented at the 15th Midwest Regional Meeting of the American Chemical Society, St. Louis, MO, Oct 1979.

[2] Taken in part from the dissertation submitted by R.J.Z. in partial fulfillment of requirements for the MS (Chem) degree, University of Missouri—St. Louis, Dec 1978.

[3] NSF Undergraduate Research Participant, Summer 1979.

[4] Semmler, F. W.; Mayer, E. W. *Chem. Ber.* 1912, *45*, 1391–97.

[5] Ruzicka, L.; Haagen-Smit, A. J. *Helv. Chim. Acta* 1931, *14*, 1122–32.

[6] Plattner, P. A.; Magyar, G. *Helv. Chim. Acta* 1941, *24*, 191–7.

[7] Takeda, K.; Minato, H. *Chem.* Pharm. *Bull* 1961, *9*, 619–25.

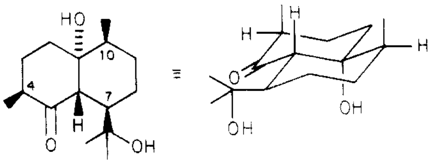
[8] Nadgouda, S. A.; Trivedi, G. K.; Bhattacharyya, S. C. *Indian J. Chem., Sect. B.* 1978, *16B*, 205–6.

0022-3263/81/1946-4309$01.25/0

paper we report our results to date.

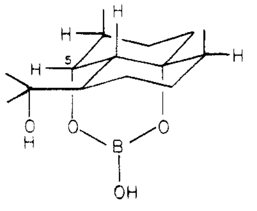
Under the conditions usually employed (alkaline aqueous acetone), the permanganate oxidation of guaiol furnishes the ketol II in only about 30% yield; other products, primarily triol IV, are also formed.[7] The procedure is difficult to scale up, due to the large quantity of manganese dioxide formed, the variable amount of permanganate consumed, and apparent pH change (decrease) during the course of oxidation. Some improvement was achieved on oxidation of guaiol with "purple benzene", but when this reaction was scaled up and the amount of crown ether used was reduced to less than 5 mol % according to the procedure described by Sam and Simmons,[9] oxidation proceeded more slowly, and the yield of II dropped significantly. In contrast, rapid oxidation at constant apparent pH and with consistent permanganate consumption was accomplished in aqueous glyme containing sodium hydroxide. Satisfactory yields were obtained; the material was identical in all respects with that obtained by oxidation in aqueous acetone.[6]

The complete stereochemistry of ketol II is shown in structures A. The *trans*-6βH ring fusion indicated was established by chiroptical measurements. Ketol II exhibited Cotton effect similar to that of several *trans*-9β*H*-1-decalones and in complete accord with the octant rule for ketones.[10] The configurations at C_4, C_7, and C_{10} (β-alkyl) are the same as those in guaiol.[11] These assignments are based on mass spectral and NMR analysis of ketol obtained by permanganate oxidation of I in heavy water. An upper limit of 10% deuterium incorporation was indicated; thus epimerization of existing asymmetric centers in I could not have occurred in the course of its transformation to II.

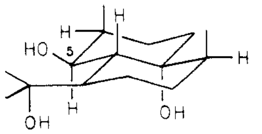


A

The stereochemical deductions summarized above were fully substantiated by studies on products obtained by treatment of II with sodium borohydride followed by acid workup.[12] Solubility differences permitted easy separation of the two reduction products: the less soluble (and higher melting) one exhibited spectral characteristics expected for the carbonyl reduction product; however, the more soluble (and lower melting) product proved to be a borate ester of a different triol. Stereochemical considerations suggest that such an ester should involve two axial C–O bonds; therefore, it can be formulated as V and the "normal" reduction product as VI. The epimeric relationship of this pair at C_5 was readily discernible in the proton NMR spectra; V exhibited a broadened signal at ca. 4.6 ppm which was unaffected by irradiation of other downfield resonances, whereas VI showed a broadened "triplet" at ca. 3.9 ppm. becoming a doublet of doublets ($J \approx 2$ and 9 Hz) on irradiation of the 5.7-ppm doublet. In the latter case, the C–H/O–H coupling evident in dry dimethyl sulfoxide was removed, leaving a pattern typical of an axial hydrogen having vicinal cis-equatorial ($J \approx 2$ Hz) and trans-axial ($J \approx 9$ Hz) neighbors.[13] It is interesting to note that V and VI were produced in almost equal amounts. Reduction of II appears to be nonstereoselective, perhaps due to the hindered nature of the carbonyl group reflected also by its reported inability to form typical ketone derivatives.[5,6]



V



VI

The facile transformation of diketone III to ketol II by treatment with base has already been alluded to, Nadgouda having obtained minor amounts of III from the sensitized photooxygenation of guaoil.[8] Furthermore, II is itself quite base sensitive, suffering dehydration rapidly and quantitatively in alcoholic solutions of alkoxides.[14] These considerations suggested that a method other than interrupted permanganate oxidation would be required to obtain III in satisfactory yields. In fact, diketone III was isolated in good yield following mild reduction of guaiol ozonolysis mixtures, specifically by catalytic hydrogenolysis or dimethyl sulfide treatment. The properties of III so formed are in general agreement with those reported[8] (see Experimental Section). Carbon-13 and proton NMR studies assure the validity of the structural assignment and in particular rule out intramolecular hemiketal isomers. The stereochemistry of III can be inferred from lack of deuterium incorporation during ozonolysis/reduction performed in methanol-*O-d* as well as by direct conversion to ketol II. Diketone III was also characterized chiroptically, exhibiting a negative Cotton effect in perhaps fortuitous agreement with that reported for other (*R*)-3-alkylcycloalkanones.[15] Considering the ease of aldol cyclization, it is probably not surprising that guaiol, ketol II, and diketone III constitute a stereochemically homogeneous group.

Experimental Section

Unless otherwise indicated, the following general information applies. Infrared spectra (IR) were recorded as potassium bromide dispersions on a Perkin-Elmer Model 337 spectrophotometer; only the major absorptions are listed. Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained on Varian T-60 and carbon spectra (^{13}C NMR) on JEOL FX100[16a] spectrometers; chemical shifts are expressed as parts per million relative to tetramethylsilane at zero. Mass spectroscopic measurements were made on an AEI MS-12 at 60 eV (or greater); the *m/e* and relative

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(9) Sam, D.; Simmons, H. *J. Am. Chem. Soc.* **1967**, *89*, 2495.

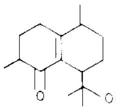
(10) Analogous cis-fused compounds exhibit negative Cotton effects similarly in agreement with the octant rule. Cf.: Djerassi, C. "Optical Rotatory Dispersion"; McGraw-Hill: New York, 1960; p 178 ff.

(11) Cf.: Minato, H. *Tetrahedron* **1962**, *18*, 365–71 and references cited therein.

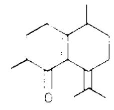
(12) The actual reducing species may be B_2H_6 generated on workup; II was recovered on treatment with LAH.

(13) Silverstein, R.; Bassler, G. C.; Morill, T. C. "Spectrometric Identification of Organic Compounds", 3rd ed.; Wiley: New York, 1974; p 191.

(14) Only a simple dehydration to enone i occurs under basic conditions; subsequent formation of dienone ii[5,6] is apparently strongly acid catalyzed.



i



ii

(15) Djerassi, C.; Krakower, G. W. *J. Am. Chem. Soc.* **1959**, *81*, 237–42.

(16) (a) Joint FT NMR facility with Washington University (St. Louis) (NSF Grant CHE-77-02068). (b) The authors acknowledge technical assistance by Mr. Bill Garrison (deceased) and Mr. Joe Kramer in measuring mass spectra. (c) We thank Professor S. Weissman for permitting use of his instrument and for his assistance in obtaining these measurements.

intensity values are indicated for major ions only.[16b] All D-line rotations were taken by using a Rudolf Model 63 polarimeter. Rotatory dispersion and circular dichroism measurements were made utilizing a JASCO model 5 ORD-CD recording spectropolarimeter.[16c]

All melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Reagents and solvents were purified by standard methods as appropriate. Microanalyses were performed by Galbraith Laboratories, Inc.; standard methods were employed to prepare analytical samples.

Guaiol (I). Guaiol was obtained from Guaiacwood Oil Concrete (Ungerer and Co.) by crystallization from methanol. Several recrystallizations afforded pure I as colorless prisms: mp 90–91 °C; $[\alpha]^{23}{}_{\mathrm{D}}$ −31° (c 4.0, alcohol) [lit.[17] colorless prisms; mp 90–91 °C; $[\alpha]^{20}{}_{\mathrm{D}}$ −30° (c 4.0, alcohol)]; ^{1}H NMR ($CDCl_3$), 1.06 (d, J = 7 Hz, 3 H), 1.08 (d, J = 7 Hz, 3 H, 1.15 (br s, 6 H), 1.2–2.8 (vbr m, ~14 H); ^{13}C NMR ($CDCl_3$) 19.8 (q), 19.9 (q), 26.0, 27.3, 27.4, 27.9, 30.9, 33.7, 33.8, 35.4, 46.3, 49.6, 73.4 (s), 138.8 (s), 139.9 (s); IR 3500–3150 (br), 1360, 1140 cm^{-1}. The mass spectrum exhibited a molecular ion at m/e (relative intensity) 222 (16) and major fragment peaks at m/e 204 (42), 161 (78), and 59 (100).

Permanganate Oxidation of Guaiol in Aqueous Acetone. The procedure reported by Takeda and Minato[7] was adapted for oxidations in aqueous acetone. Yields of ketol II were variable. In one of the more successful experiments, a solution of 4.8 g (30 mmol) of $KMnO_4$ in 100 mL of water was added in small portions to a solution of 3.33 g of guaiol (15 mmol) dissolved in 150 mL of acetone containing 1.5 mL of 2 N NaOH, and the reaction mixture was maintained at 23 °C. Decolorization of permanganate and precipitation of manganese dioxide was noted during the entire 0.5-h addition period. Thereafter, the mixture was treated with 15 g of sodium bisulfite, and the residual manganese dioxide was filtered and washed with acetone. The filtrate and washings were combined, and the volatiles were removed in vacuo. The remaining aqueous layer was extracted several times with $CHCl_3$ (ca. 800 mL total), the combined extracts were dried over Na_2SO_4, and the solvent was evaporated, leaving 4.0 g of a viscous yellowish oil which contained some crystalline material. Addition of 20 mL of ether, filtration, and washing with more chilled ether furnished 2.85 g (75%) of II, mp 215–218 °C. Several recrystallizations from methanol gave pure ketol II, mp 224–225 °C (lit.[6] mp 224–225 °C).

Attempts to scale up the production of II resulted in an appreciable decline in yield. In one such attempt 30.0 g of guaiol (0.13 mol) dissolved in 2000 mL of acetone and 800 mL of water containing 5 mL of 1 N NaOH was treated with 60 g of pulverized $KMnO_4$ (0.38 mol); the progress of the reaction and the workup were similar to those described above. Crystallization of the crude reaction product (36.5 g of a mixture of oil and a crystalline substance) from methanol furnished only 11.2 g (34%) of II (mp 217 °C) identical to II from previous runs (IR).

Ketol II, purified by repeated crystallization from methanol and dried in vacuo, was characterized by the following physical and spectroscopic properties: mp 224–225 °C; $[\alpha]^{23}{}_{\mathrm{D}}$ +50° (c 1.22, alcohol) [lit.[6] colorless plates; mp 224–225 °C; $[\alpha]^{23}{}_{\mathrm{D}}$ +50° (c 1.22, alcohol)]; ^{1}H NMR (Me_2SO–d_6) 0.90 (d, J = 7 Hz, 3 H), 0.95 (d, J = 7 Hz, 3 H), 1.02 (s, 3 H), 1.07, (s, 3 H), 1.2–2.2 (vbr m, ~12 H), 4.02 (s, ~1 H, D_2O exchangeable), 4.05 (s, ~1 H, D_2O exchangeable); ^{13}C NMR (Me_2SO–d_6) 13.6, 14.6, 21.1, 22.7, 28.9, 30.9, 30.9, 32.4, 38.6, 39.2, 49.5, 55.4, 71.4, 77.3 ppm (excluding the carbonyl carbon); IR 3550–3250 (br), 1705, 995 cm^{-1} (lit.[7] IR 3430, 1705, 995 cm^{-1}). The mass spectrum showed a molecular ion t m/e (relative intensity) 254 (1.9) and major peaks at m/e 236 (28), 218 (100), 203 (40), and 150 (30). The ORD exhibited a positive cotton effect with molecular rotations as follows: $[\phi]_{298}$ +329, $[\phi]_{272}$ 0°, $[\phi]_{264}$ −22°, molecular amplitude 351°; in the CD spectrum maximum molecular elepticity was at 284 nm, $[\theta]_{284}$ +4456, $w_{1/2}$ = 34 nm (c 1.14 × 10^{-3} g/mL, methanol).

Triol IV was also isolated in some runs; in one attempt, the initial ether mother liquor was allowed to partially evaporate, giving crystals melting at 104–105 °C (lit.[7] mp 105–107 °C): IR 3385, 1135, 1010, 897, 815 cm^{-1} (in agreement with literature values[7]).

In other experiments, the following observations were made regarding permanganate oxidation of I in alkaline aqueous acetone: (a) the pH of the reaction mixture (initially 8) decreased (final value of 6.5 as determined by short-range paper) during the reaction; (b) up to 100% more than a stoichiometric amount of $KMnO_4$ relative to guaiol was require to achieve an "excess" (lasting purple color); (c) "incomplete" oxidation was observed, and 20–30% triol IV (crude yield based on guaiol) was obtained in some runs even with "excess" permanganate.

Permanganate Oxidation of Guaiol with Purple Benzene. A solution of 0.45 g of guaiol (2.0 mmol) in 20 mL of benzene was treated with 1.11 g of dicyclohexyl-18-crown-6 (3 mmol) and 0.48 g of $KMnO_4$ (3 mmol) contained in 250 mL of benzene. The reaction mixture was maintained at room temperature during the 0.25-h addition period: manganese dioxide formation was evident immediately; complete permanganate decolorization required less than 2 h. A solution of sodium bisulfite (2 g) in water (200 mL) was added, and the benzene layer was separated and dried over Na_2SO_4. Evaporation left a yellow oil (1.7g) from which 0.40 g (78%) of ether-insoluble solid identified as ketol II by melting point (195–220 °C) and IR was obtained.

Attempts to oxidize guaiol by using $KMnO_4$ in benzene containing less than a stoichiometric amount of crown ether were less successful. In one such attempt 7.55 g of guaiol (0.034 mol), 14.3 g of $KMnO_4$ (0.090 mol), 1.20 g of dicyclohexyl-18-crown-6 (0.003 mol), and 1 L benzene were rolled in a ball mill for 22 h. Workup gave a yellowish oil (7.0 g) from which 4.2 g of ether-insoluble product identified as mostly ketol II by IR was obtained (48%).

Permanganate Oxidation of Guaiol in Aqueous Glyme. A well-stirred solution of 1.67 g of guaiol (7.5 mmol) in 60 mL of glyme with 10 mL of water added and at pH 8.0–8.5 (0.1 N NaOH) was treated portionwise with 0.44 M aqueous $KMnO_4$, with the mixture maintained at 25–30 °C. After 30 mL (13 mmol) of the $KMnO_4$ solution had been added, decolorization slowed considerably; addition was continued until a lasting excess was noted (color not consumed after 0.5 h). A total of 40 mL (18 mmol) of solution was added. Thereafter, the excess permanganate was destroyed by addition of sodium bisulfite, the mixture was filtered through asbestos to remove manganese dioxide, and the residue and filter were washed with warm glyme (50 °C). The clear colorless glyme–water solution was evaporated to dryness in vacuo and the amorphous solid residue first leached several times with ether and then exhausted with boiling methanol (insoluble salts removed by filtration). The clear colorless methanol solution was evaporated to dryness, leaving 1.35 g of solid (mp 208–210.5 °C) identified as ketol II by IR (70% crude yield). Several recrystallizations from methanol furnished pure II, mp 223–224 °C.

Evaporation of the ether washings (above) gave 0.560 g of solid (mp 97.5–99 °C) identified as triol IV (30% crude yield). Several crystallizations from anhydrous ether gave pure IV: mp 101.5–102.5 °C; ^{1}H NMR ($CDCl_3$) 0.89 (d, J = 7 Hz, 3 H), 1.00 (d, J = 7 Hz, 3 H), 1.07 (s, 3 H), 1.20 (s, 3 H) 1.3–2.3 (vbr m, 13 H), 2.52 (br s, 3 H, D_2O exchangeable); IR 3575–3050, (br), 1135, 1010, 897, 815 cm^{-1} (same as reported).[7]

Permanganate oxidation of guaiol in the presence of D_2O was carried out as follows: 0.270 g of guaiol (1.22 mmol) in 15 mL of dry glyme was titrated with a solution of 0.700 g of $KMnO_4$ in 10 mL of D_2O containing K_2CO_3 (2.5 mg). A workup as indicated above (trituration with boiling glyme instead of methanol) gave 0.175 g (50%) of crude II (mp 208.5–21 °C) which was recrystallized from methanol[18] to give pure ketol II, mp 220.5–221.5 °C. The mass spectrum of this sample was essentially identical with that of II prepared in normal water, exhibiting the parent ion at m/e (relative intensity) 254 (1.4) and fragment ions at 236 (30), 218 (100), 203 (51), 178 (39), 175 (39), 161 (33), and 150 (51). The ^{13}C NMR spectrum of this sample of ketol showed no evidence of C–D coupling.

Ozonolysis of Guaiol. A solution of 1.00 g (4.50 mmol) of guaiol in 200 mL of methanol cooled in dry ice/acetone was treated with ozone (ca. 0.2 mmol/min in O_2) until a blue color appeared in solution (about 0.5 h). Thereafter, the solution was flushed with oxygen until colorless and then with argon for 0.25 h while cooling was maintained. [This solution gave a positive test with KI and showed one major component, relative R_f 0.66 on TLC analysis (3% $CH_3OH/CHCl_3$); the IR of an aliquot carefully

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(17) Simonsen, J.; Barton, D. H. R. "The Terpenes"; Cambridge University Press: Cambridge, 1952; Vol. III, p 156 ff.

evaporated to dryness exhibited strong absorption at 1700 cm^{-1}, while the ^{1}H NMR lacked the resonance expected of a C–OCH$_3$ group.[19]] One of two methods was employed for reduction of this solution.

Method A. The cold solution obtained on ozonolysis of 1.00 g (4.50 mmol) of guaiol was poured onto 0.50 g of 5% Pd/C, prepared for hydrogenation, and stirred in an atmosphere of H$_2$ overnight, while being allowed to slowly warm to room temperature. (In a separate experiment 70–80% of the theoretical H$_2$ uptake was observed to occur within 2 h at -70 °C.) The catalyst was filtered through Celite, and the solution so obtained was tested with potassium iodide (negative) and analyzed by TLC (3% CH$_3$OH/CHCl$_3$, one major component, relative R_f ~1.0). Careful evaporation of the solvent left a thick yellow oil (1.08 g), which on crystallization from ether/hexane gave III: mp 63.5–66.0 °C; 0.830 g (72%).

Method B. The cold mixture containing the ozonolysis product from 1.17 g of guaiol (5.27 mmol) was treated with 3.9 mL of dimethyl sulfide (53 mmol) and the stirred solution allowed to warm slowly to room temperature overnight. Thereafter, the solvent was carefully removed in vacuo, leaving a viscous yellow oil (including Me$_2$SO). This oil was taken up in hexane, with enough ether to achieve complete solution, and water was added to the point of cloudiness; cooling gave of diketone III: 1.00 g (74%); mp 65–66 °C (identical with the hydrogenolysis product described above.

An analytical sample of III was prepared by repeated recrystallization from ether/hexane. Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 71.43; H, 10.44. Diketone III, purified by recrystallization from anhydrous ether and dried in vacuo overnight, was characterized by the following properties: mp 65.5–66.5 °C; $[\alpha]_D$ -41° (*c* 0.52, alcohol) [lit.[8] mp 65–66 °C; showed no rotation]; ^{1}HNMR (CDCl$_3$) 1.04 (d, $J \approx 7$ Hz, 3 H shifted to 1.07 in the presence of 4 mol % of Eu(fod)$_3$), 1.06 (d, *J* ' 7 Hz, 3 H, shifted to 1.21), 1.10 (s, 3 H, shifted to 1.27), 1.23 (s, 3 H, shifted to 1.39), 1.3–3.2 (complex m and D$_2$O- exchangeable s, ~14 H total) [lit.[8] 1.05 (d) 1.07 (d), 1.1 (s), 1.22 (s), 2.18 (D$_5$O exchangeable); solvent not indicated]; ^{13}C NMR (CDCl$_3$) 17.1 (q), 18.8 (q), 24.6 (q), 27.0 (t), 27.9 (q), 28.5 (t), 30.1 (t), 34.5 (t), 42.1 (d), 44.0 (d), 44.1 (t), 49.0 (d), 72.1 (s), 216.5 (s), 217.9 (s); IR 3500–3320 (br), 2950, 2875, 1675, 1460, 1420, 1375, 1320, 1280, 1185, 1145, 1130, 1117, 1042, 947 cm^{-1} (same as that reported[8]). The mass spectrum of III showed a molecular ion at *m/e* (relative intensity) 254 (0.8) and major fragments at 236 (10) 221 (7.5) 218 (8), 203 (8), 196 (17), 95 (57), 59 (62), 55 (73), 43 (82), and 41 (100); however, the fragmentation pattern proved very sensitive to purity of sample, inlet temperature, and impact voltage. The ORD spectrum of III (*c* 2.98 × 10^{-4} g/mL, CH$_3$OH) exhibited a negative Cotton effect with molecular rotations as follows: $[\phi]_{319}$ -2268°, $[\phi]_{305}$ 0°, and $[\phi]_{276}$ +8433°, *a* = -10 700°.

Ozonolysis of guaiol in methanol-*O-d*, followed by hydrogenolysis over Pd, gave III without apparent deuterium incorporation (mass spectral analysis).[18]

Isomerization of Diketone III. A solution of 0.325 g of pure dry III was prepared in 20 mL of methanol. Water was added (25 mL) and the mixture concentrated to near dryness at 45–50 °C in vacuo. More water was added, dissolution was effected by sonication, and the mixture was cooled after evaporation to half-volume in vacuo at 45–50 °C. Repeating this procedure produced three successive crops of crystalline material: first crop, 0.048 g (14%), mp 65–75 °C, resolidifying and remelting 200–220 °C, a mixture of diketone III and ketol II (TLC and IR); second crop, 0.120 g (34%), mp 217–220 °C, ketol II (IR); third crop, 0.139 g (39%), mp 221–222 °C, ketol II (IR).

Reduction of Ketol II. To a solution of 5.0 g of ketol II (20 mmol) in 300 mL of 95% ethanol was added 5 mL of 0.1 N NaOH and 6.0 g (16 mmol) of sodium borohydride. The mixture was stirred at 23 °C for 115 h, after which time the excess hydride was destroyed by addition of 40 mL of 3 N HCl solution. The mixture was then evaporated in vacuo to about one-third of its original volume and poured into 500 mL of water. The aqueous mixture was extracted with chloroform (ca. 1 L), and the extract was dried over sodium sulfate and evaporated under reduced pressure, leaving 5.2 g of a white crystalline material melting at 134–140 °C (with gassing). The infrared spectrum of this material indicated the complete absence of the ketonic absorption at 1705 cm^{-1}. The crude product was crystallized from acetone to give 1.6 g of a white crystalline material, VI, melting at 189–192 °C. Subsequent recrystallization from acetone gave an analytical sample: mp 200–201 °C; $[\alpha]^{23}{}_D$ +30° (*c* 0.25, alcohol); ^{1}H NMR (Me$_2$SO-d_6) 0.90 (d, *J* = 7, 3 Hz), 0.95 (d, *J* = 7 Hz), 1.15 (br s, 6 H), 1.2–2.2 (m, ~12 H), 3.2–4.0 (vbr t, $J \approx 8$ Hz, 1 H; collapsing to 3.80, dd, $J \approx 2, 9$ Hz, on irradiation at 5.70), 4.15 (b, 1 H, D$_2$O exchangeable), 5.70 (br d, $J \approx 6$ Hz, 1 H, D$_2$O exchangeable), 6.00 (br, 1 H, D$_2$O exchangeable); IR$_{max}$ 3250 (br), 1460, 985, 878 cm^{-1}. The mass spectrum showed a molecular ion at *m/e* (relative intensity) 256 (s) and major peaks at 238 (10), 220 (8), 205 (10), 180 (94), 162 (58), 127 (76), and 43 (100). Anal. Calcd for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 69.82; H, 11.25.

The acetone mother liquor of triol VI was evaporated in vacuo, and the residue was recrystallized from methylene chloride, furnishing 1.9 g of V as colorless crystals melting at 171–173 °C (with gassing) and which flamed green on a porcelain spatula. Subsequent recrystallization from methylene chloride containing a trace of acetone afforded an analytical sample: mp 174–175 °C; ^{1}H NMR (Me$_2$SO-d_6) 0.85 (d, *J* = 7 Hz, 3 H), 0.95 (d, *J* = 7 Hz, 3 H), 1.05 (s, 3 H), 1.08 (s, 3 H), 1.1–2.2 (br ~12 H), 4.25 (s, 1 H), 4.6 (br, 1 H, D$_2$O exchangeable), 5.8 (s, ~1 H, indistinguisheable from CH$_2$Cl$_2$), 7.05 (s, 1 H, D$_2$O exchangeable); IR$_{max}$ 3400 (br), 1410, 890, 868, 845, 805 cm^{-1}. The mass spectrum showed major peaks at *m/e* (relative intensity) 264 (11), 349 (5), 235 (2), 224 (100), 182 (39), 162 (55). (A mass spectrum of the volatiles obtained on warming VI slowly to 150 °C displayed promiment peaks at *m/e* 84 and 35.) Anal. Calcd for $C_{15}H_{27}O_4B \cdot 0.5CH_2Cl_2$: C, 57.37; H, 8.63. Found: C, 57.76; H, 8.81.

Partial evaporation of the initial methylene chloride mother liquor yielded additional crops: 0.8 g, mp 165–168 °C (gassing); 0.35 g, mp 160–164 °C (gassing). Infrared spectra of both the second and third crops indicated an approximately 1:1 mixture of reaction products V and VI.

Attempts to effect reduction of II with lithium aluminum hydride proved unsuccessful. In one experiment unchanged ketol II was recovered (85%) even after 24 h of reflux with excess LAH in THF.

Registry No. I, 489-86-1; II, 78854-21-4; III, 67697-24-9; IV, 78804-76-9; V, 78804-77-0; VI, 78804-78-1.

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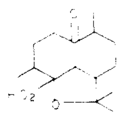
[18] Appropriate control experiments were performed to assure that washout of carbon-bound deuterium does not accompany purification by recrystallization.

[19] The product of ozonolysis appears to be in part the intramolecular alkoxy hydroperoxide iii since Fe(II)/Cu(II)-induced decomposition gives a γ-lactone (IR 1740 cm^{-1}).



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