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THE SYNTHESIS AND SELECTIVE DEGRADATION OF GUAIOL

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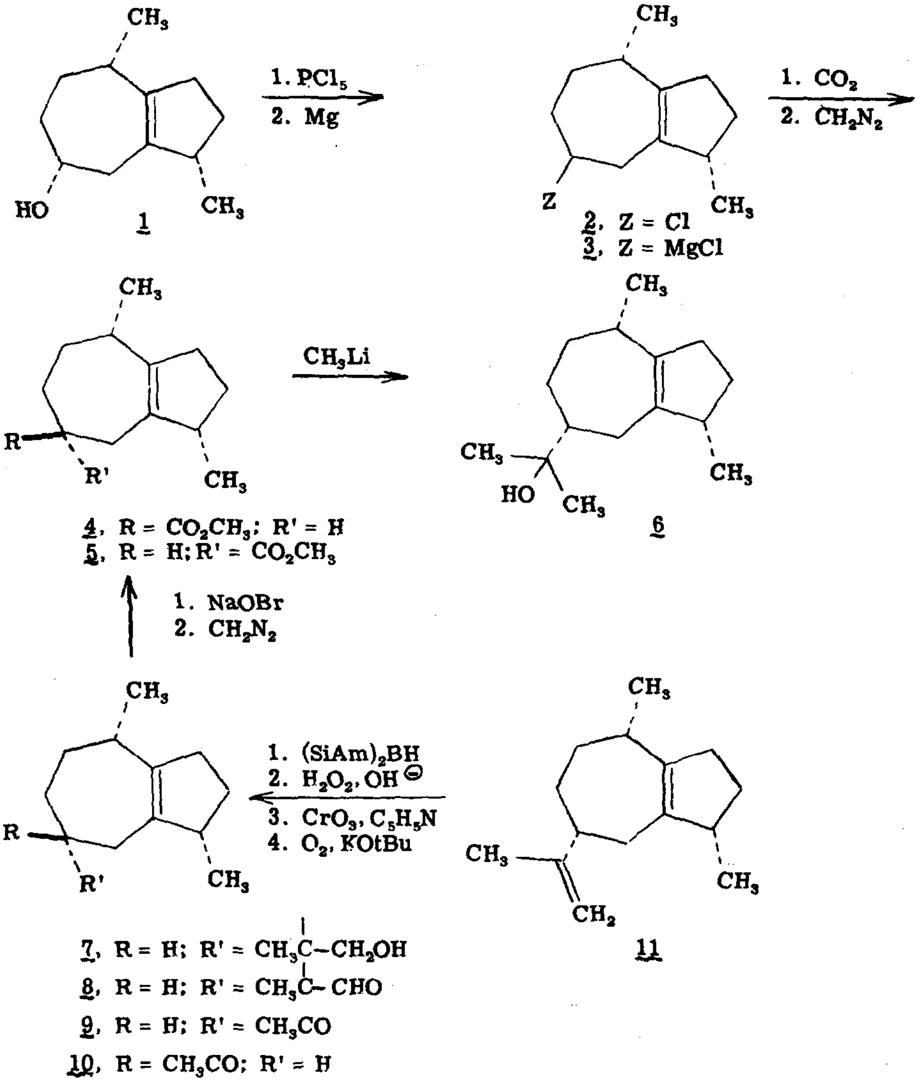
In the previous report we described the stereoselective synthesis of the acetate derivative of alcohol **1** *via* acetolysis of a 7a-methanesulfonoxymethylhydrindane. This letter describes the conversion of alcohol **1** to an ester mixture **4** and **5** also obtained *via* degradation of guaiol (**6**) and the reconversion of ester **5** to guaiol thus completing a formal total synthesis of that substance.

Alcohol **1** upon treatment with PCl_5 afforded the chloride **2**. Conversion to the Grignard reagent **3** followed by carbonation and esterification afforded a roughly 2:1 mixture of the esters **4** and **5**.[3] Equilibration of this mixture in refluxing methanolic sodium methoxide led to a 55:45 mixture of these epimers.

Roughly the same mixture of esters **4** and **5** [λ_{max}^{film} 5.77, 7.02 and 8.62μm; $\delta_{TMS}^{CCl_4}$ 3.56 (CH_3O), and 1.15-0.88 (CH_3 doublets)] was secured from guaiol (**6**)[4] *via* the following sequence. Pyrolysis of the acetate derivative[5] afforded α-guaiene (**11**).[6] Selective hydroboration of this diene with disiamylborane[7] followed by oxidation led to alcohol **7** [λ_{max}^{film} 3.02, 6.98, and 9.72μm; $\delta_{TMS}^{CDCl_3}$ 3.58 (CH_2O-pair of doublets), 1.38 (OH), 1.00 (CH_3 doublet, J = 7 Hz), 0.96 (CH_3 doublet, J = 7 Hz), and 0.90 ppm (CH_3 doublet, J = 6 Hz)]. Oxidation using Collins' bispyridine chromium oxide reagent[8] in methylene chloride afforded the aldehyde **8** [λ_{max}^{film} 3.72, 5.80, 6.90, 7.20, and 7.34μm; $\delta_{TMS}^{CCl_4}$ 9.56 (CHO doublet, J = 1 Hz), 1.02 (CH_3 doublet, J = 7 Hz), 1.00 (CH_3 doublet, J = 7 Hz), 0.97 (CH_3 doublet, J = 6 Hz)]. A solution of this



1

2, Z = Cl
3, Z = MgCl

4, R = CO_2CH_3; R' = H
5, R = H; R' = CO_2CH_3

6

7, R = H; R' = $CH_3\overset{|}{C}-CH_2OH$
8, R = H; R' = $CH_3\overset{|}{C}-CHO$
9, R = H; R' = CH_3CO
10, R = CH_3CO; R' = H

11

aldehyde in KOH-t-BuOH upon vigorous stirring under an oxygen atmosphere[9] underwent further oxidation to a roughly 1:1 (equilibrium) mixture of ketones 9 and 10 [λ_{max}^{film} 5.85 and 8.61μm; $\delta_{TMS}^{CCl_4}$ 2.06 (CH_3CO), 2.05 (CH_3CO), and 1.12-0.84 ppm (CH_3 doublets)]. Oxidation of this mixture with bromine in aqueous dioxane-NaOH afforded a mixture of acids whose subsequent treatment with diazomethane gave a roughly 85:15 mixture of esters 5 and 4, respectively, in 30% overall yield. Evidently, the hypobromite oxidation of ketones 9 and 10 to the corresponding acids proceeds more readily with the former epimer.[10] Upon treatment with refluxing methanolic sodium methoxide the 85:15 ester mixture was slowly converted to a nearly 1:1 mixture whose spectral and chromatographic properties were indistinguishable from the aforementioned equilibrium mixture of synthetic esters. Isolation of the initially predominant ester 5 by preparative gas chromatography followed by treatment with methyllithium afforded natural guaiol 6 [m.p. 82-85° λ_{max}^{KBr} 3.00, 7.37, 8.69, 8.70, 10.03, 10.41, 10.80, 10.97, 11.36, and 12.18μm; $\delta_{TMS}^{CDCl_3}$ 1.18 (isopropylol CH_3's), 0.98 (CH_3 doublet, J = 7.5 Hz), and 0.96 ppm (CH_3 doublet, J = 7 Hz)].

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4. We are indebted to Prof. R. B. Bates for a sample of Guiacum Wood Oil from which this material was secured.
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10. A considerable residue remained after distillation of the ester mixture. Presumably this residue contained brominated products.