Experimental Section

Method of Analyses.—Nmr spectra were recorded on either a Varian Model A-60 or HA-100 resonance spectrometer. The infrared spectra were obtained on a Beckman Model IR-10 infrared spectrophotometer.

Starting Materials. Starting Olefins.—The 3,3-dimethyl butene, *trans*-piperylene, and acenaphthylene were obtained from Columbia Organic Chemicals Co. Styrene, butadiene, and isobutylene are Matheson Co. products. The acenaphthylene was recrystallized three times from hexane, mp 92–93°. Butadiene of +95% purity and isobutylene of 99% purity were used as such. All other starting materials were distilled prior to their use.

Acetylthiosulfenyl Chloride.—To a stirred solution of 37.5 g (0.25 mole) of diacetyl disulfide[12] in 50 ml of dry methylene chloride 33.75 g (0.25 mole) of freshly distilled sulfuryl chloride was slowly added. The reaction was carried out under a nitrogen atmosphere and the reaction temperature kept at 10–15°. After the addition was completed, the mixture was stirred for 1.5 hr at ambient temperature. The progress of the reaction can be conveniently followed by nmr analysis. The following singlets were observed: diacetyldisulfide (2.50 ppm), acetylthiosulfenyl chloride (2.67 ppm), acetyl chloride (2.63 ppm). The acetyl chloride and solvent were removed on a rotary evaporator at ambient temperature (15 mm), thus affording 35 g (*ca.* 98% yield) of acetylthiosulfenyl chloride. Nmr analysis of the product indicated *ca.* 1% of the starting disulfide and no other impurities.

General Procedures for the Addition of Acetylthiosulfenyl Chloride to Unsaturates.—Acetylthiosulfenyl chloride was slowly added to a stirred 50% solution of the unsaturate in methylene chloride containing about 0.5% of suspended $CaCO_3$. Anhydrous reaction conditions were employed. Mole ratios of the reactants and reaction temperatures are tabulated in Table I.

The addition reaction is exothermic and very rapid. After the addition was completed, the reaction mixture was stirred at the reaction temperature for an additional 15–30 min, then the solvent and possible excess of the unsaturate were removed at 0° (2 mm). Nmr analysis of the crude product provided the isomer distribution (Table I) and conversion data to the adducts of >95%. The conversion was also confirmed by the weight of the crude product. Part of the product was purified by fractional distillation *in vacuo* which afforded samples for elemental analysis.

Registry No.—I, 13250-14-1; II, 13250-15-2; III, 13250-16-3; IV, 13250-17-4; V, 13250-18-5; VI, 13270-33-2; VII, 13270-34-3; VIII, 13250-19-6; IX, 13250-20-9; acetylthiosulfenyl chloride, 13250-24-3.

Acknowledgment.—The authors wish to thank W. C. Whitlock for excellent technical assistance and Dr. J. R. J. Reed for obtaining the 100-Mc nmr data.

[12] Diacetyl disulfide was prepared *via* oxidation of thiolacetic acid with dimethyl sulfoxide.

3-Hydroxydamsin, a New Pseudoguaianolide from *Ambrosia Psilostachya* DC (Compositae)

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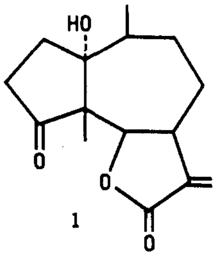
An investigation[2] of the infraspecific variation of sesquiterpene lactones in the Compositae species *Ambrosia psilostachya* DC has led to the isolation and structure determination of a new pseudoguaianolide, which we named 3-hydroxydamsin. Chloroform extraction of plant material from central Texas yielded two pseudoguaianolides of known structures, coronopilin (**1**) and parthenin (**2**), in addition to the new substance, 3-hydroxydamsin (**3**), $C_{15}H_{20}O_4$.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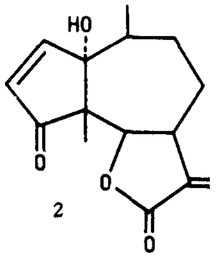
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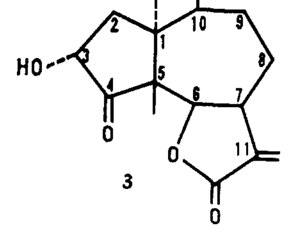

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The spectral data suggested that the new sesquiterpene lactone contained several functional groups typically found in pseudoguaianolides: an α,β'-unsaturated γ-lactone [λ_{max} 212 mμ (ϵ 9400); infrared bands at 1750 (carbonyl) and 1660 cm^{-1} (double bond); and nmr signals at δ 4.74[3] (doublet, J = 9 cps, for the C-6 lactonic proton), 3.4 (multiplet for the C-7 proton), 5.59 and 6.30 (two doublets, J = 3 cps, for the C-11 methylene group protons)]; a 5-ring keto group [λ_{max} 308 mμ (ϵ 38) and the strong infrared band at 1750 cm^{-1} which was in accord with the presence of two carbonyl functions]; a C-5 tertiary methyl group [nmr singlet at δ 1.12]; a C-10 secondary methyl group [nmr doublet at δ 1.10, J = 6 cps]; and a secondary hydroxyl group [infrared band at 3500 cm^{-1}; nmr in deuteriochloroform, a double doublet at δ 4.37 (J = 7 and 2.5 cps, for the C-3 proton; in deuterated dimethyl sulfoxide, a doublet at δ 5.54 (J = 5 cps, for the hydroxyl proton)].

The new pseudoguaianolide (**3**) was transformed on silica gel into an isomeric $C_{15}H_{20}O_4$ substance to which we assigned structure **4**, in part, on the basis of the spectral data [λ_{max} 211 mμ (ϵ 9600) and 290 (45); infrared bands at 3530, 1750, and 1660 cm^{-1}; nmr in deuteriochloroform, the spectrum was similar to the one obtained for **3** with the exception that the δ 4.37 double doublet was replaced by a singlet at 4.13, which can be ascribed to the C-4 proton; in deuterated dimethyl sulfoxide, the δ 4.13 singlet disappeared and two new doublets (J = 5.5 cps) were observed at 3.98 (C-4 proton) and 5.05 (C-4 hydroxyl proton)]. Compound **4** was synthesized from damsin (**5**)[4] by bromination with trimethylaniline perbromide,[5] followed by an alkaline treatment. Based on the obvious relationship between

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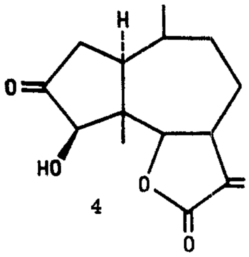
[1] National Institutes of Health Pre-doctoral Trainee, 1964–1967, Grant 511 GM-789.

[2] For recent investigations on the sesquiterpene lactones in this species, see (a) T. J. Mabry, H. E. Miller, H. B. Kagan, and W. Renold, *Tetrahedron*, **22**, 1139 (1966); (b) T. J. Mabry, W. Renold, H. E. Miller, and H. B. Kagan, *J. Org. Chem.*, **31**, 681 (1966); (c) H. B. Kagan, H. E. Miller, W. Renold, M. V. Lakshmikantham, L. R. Tether, W. Herz, and T. J. Mabry, *ibid.*, **31**, 1639 (1966).

[3] All chemical shift values are reported in parts per million (δ scale).

[4] For a discussion of the stereochemical features shown in **5** for damsin, see T. J. Mabry, H. B. Kagan, and H. E. Miller, *Tetrahedron*, **22**, 1943 (1966).

[5] A. Marquet and J. Jacques, *Bull. Soc. Chim. France*, 90 (1963).



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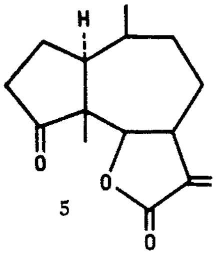
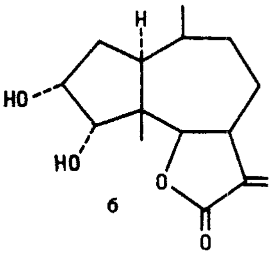


5

3-hydroxydamsin and its silica gel derived isomer, the synthesis of the latter substance from damsin provided structures **3** and **4**, respectively, for the two $C_{15}H_{20}O_4$ compounds, with the exception of the stereochemical orientations of their hydroxyl groups.

The final proof of structure for 3-hydroxydamsin was provided by its synthesis from ambrosiol (**6**). When ambrosiol was oxidized with dimethyl sulfoxide and 1.5 equiv of acetic anhydride,[6] the product mixture consisted of 3-hydroxydamsin, ambrosiol, and two new substances, to which we assigned structures **7** and **8**, in the approximate ratio 1:1:6:1, respectively. The synthesis of 3-hydroxydamsin from ambrosiol, albeit in low yield, establishes its structure as **3**. Furthermore, the new $C_{15}H_{20}O_4$ product from the oxidation of ambrosiol can be assigned structure **7** on consideration of the spectral data [λ_{max} 209 mμ (ε 8,000) (α,β′-unsaturated γ-lactone), 309 (35) (keto group); infrared bands at 3400 (hydroxyl), 1750 (five-ring keto group and γ-lactone), and 1650 cm^{-1} (double bond); nmr in deuteriochloroform, singlet at δ 3.52 (C-4 proton); in deuterated dimethyl sulfoxide, doublet (J = 5 cps) at δ 6.21 (hydroxyl proton)]. Because this new substance must have the same configuration for the C-4 hydroxyl group as in ambrosiol (**6**), it can be assigned structure **7**. Thus the C-4 hydroxyl group in the product from the silica gel isomerization of 3-hydroxydamsin can be assigned a β configuration as shown in **4**.



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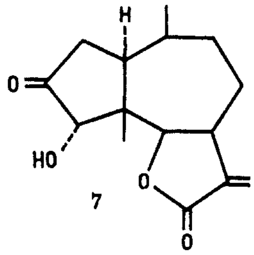

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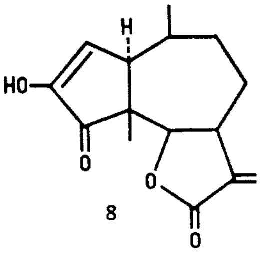

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The third product which was obtained from the dimethyl sulfoxide–acetic anhydride oxidation of ambrosiol was a $C_{15}H_{18}O_4$ substance to which we assigned structure **8** [λ_{max} 260 mμ (ε 6600) (keto enol function), 210 (ε 9000) (α,β′-unsaturated γ-lactone); infrared bands at 3200 (hydroxyl), 1725 and 1700 (carbonyls), and a sharp band at 1630 cm^{-1} (double bonds)]. The nmr spectrum of the keto enol compound (**8**) in deuterated dimethyl sulfoxide exhibited a double doublet at δ 2.90 (J = 5 and 2 cps) for the C-1 allylic proton, a doublet at 6.27 (J = 2 cps) for the C-2 double bond proton, and a singlet at 9.45 for the C-3 hydroxyl proton. The latter signal disappeared on addition of deuterium oxide to the nmr tube. Compound **8** was the only product from the oxidation of ambrosiol when excess acetic anhydride was employed.

The isolation of 3-hydroxydamsin from two populations of *A. psilostachya* DC represents yet another example of infraspecific variation of the sesquiterpene lactone chemistry in this species. The three dilactone pseudoguaianolides,[2] psilostachyin, psilostachyin B, and psilostachyin C, which occur in Gulf Coast populations of *A. psilostachya*, have also been found in approximately a 3:6:2 ratio in Vera Cruz, Mexico, populations of *A. cumanensis* Kunth.

Experimental Section[7]

Isolation of 3-Hydroxydamsin (3).—A collection of *Ambrosia psilostachya* DC, voucher no. 242621,[8] was obtained 20 miles northwest of Austin, Texas, Nov 7, 1965. The air-dried ground plant material (100 g) was extracted with chloroform and worked up in the usual manner[2] to yield 3.3 g of a thick syrup. Nmr analysis indicated the presence of 0.52 g of coronopilin (**1**), 0.06 g of parthenin (**2**), and 0.42 g of the new sesquiterpene lactone, 3-hydroxydamisin (**3**). The crude syrup was chromatographed over silica gel. Elution with 10% ethyl acetate in chloroform afforded fractions containing 3-hydroxydamsin and an equal amount of another new substance not previously detected in the crude syrup. Later fractions contained coronopilin, coronopilin mixed with parthenin, and, finally, pure parthenin. After recrystallization of the crude material from methylene dichloride–diisopropyl ether, pure samples of coronopilin, mp 178–180°, and parthenin, mp 164–166°, were obtained, which were shown to be identical with authentic samples by nmr and mixture melting points. The fractions containing 3-hydroxydamsin (**3**) and the new compound (**4**) were combined. It was observed that the two compounds were separated on silica gel G tlc plates using ether as the developing solvent: R_f 0.24 for **3** and 0.04 for **4**. The combined fractions containing **3** and **4** were chromatographed over a column of thin layer silica gel G. When the column was eluted with ether, the first fractions contained 3-hydroxydamsin, which crystallized after evaporating the ether and triturating the syrup with ether. Pure **3** (65 mg) was obtained on recrystallization of the crude material from hot benzene: mp 142–145°; $[\alpha]^{24}\mathrm{D}$ +2.7° (c 1.5, $CHCl_3$); ultraviolet (MeOH), λ_{max} 212 mμ (ε 9400) and 308 (38); infrared bands ($CHCl_3$) at 3500 (hydroxyl), 1750 (keto and γ-lactone), and 1660 cm^{-1} (double bond).

Compound **4** crystallized when the ether was allowed to evaporate from the later fractions from the silica gel column. Pure **4** (75 mg) was obtained on recrystallization of the crude material from chloroform–ether: mp 147–148°; $[\alpha]^{24}\mathrm{D}$ −197° (c 1.21, $CHCl_3$); ultraviolet (MeOH), λ_{max} 211 mμ (9600) and 290 (45); infrared bands ($CHCl_3$) at 3530, 1750, and 1660 cm^{-1}.

Anal. for **3**. Calcd for $C_{15}H_{20}O_4$: C, 68.18; H, 7.58; O, 24.42. Found: C, 68.30; H, 7.72; O, 24.13; mol wt (mass spectrum), 264.

Anal. for **4**. Calcd for $C_{15}H_{20}O_4$ (given above). Found: C, 68.40; H, 7.55; O, 24.26; mol wt (mass spectrum), 264.

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(6) J. D. Albright and L. Goldman, *J. Am. Chem. Soc.*, **87**, 5661 (1965).

(7) All melting points are uncorrected. Analyses were determined by Dr. Alfred Bernhardt, Max-Planck Institut für Kohlenforschung, Mülheim, West Germany.

(8) All voucher specimens are deposited in the University of Texas Herbarium, Austin, Texas. Two Vera Cruz, Mexico, collections of *A. cumanensis* Kunth were made on Aug 20, 1965 (voucher no. 248427) and May 14, 1966 (voucher no. 247278).

Conversion of 3-Hydroxydamsin (3) to 4.—A solution of 13 mg of **3** in 10 ml of methylene dichloride was mixed with 2 g of thin layer silica gel G and dried. After 8 days, the silica gel was eluted with methanol. An nmr analysis of the syrup obtained on evaporating the methanol indicated a 1:1 mixture of **3** and **4**. The compounds were separated on a column of thin layer silica gel. Elution of the column with ether gave initially a fraction which yielded 3 mg of **3** and a later fraction which afforded 4 mg of **4**. Both compounds were obtained crystalline and were identical by tlc, nmr, and melting point with the materials previously isolated.

Synthesis of 4.—A solution of damsin (**5**, 110 mg) and trimethylaniline perbromide (167 mg, 1 equiv) in 10 ml of tetrahydrofuran was allowed to stand at room temperature. The crystals of trimethylaniline bromide which formed were filtered and the filtrate was concentrated to a syrup. Nmr analysis of the crude syrup indicated a 1:1 mixture of damsin and another compound, presumably 3-bromodamsin. The syrup was dissolved in 5 ml of dimethyl sulfoxide and mixed with 5 ml of 0.75 *N* potassium hydroxide. After the solution had warmed for 1 hr on a steam bath, it was acidified with hydrochloric acid and extracted with chloroform. The syrup obtained on evaporating the chloroform was chromatographed over silica gel. Elution of the column with ether afforded first damsin, then damsin mixed with **4**, and finally fractions containing **4**. The latter fractions afforded 15 mg of crystals, mp 147–148°, which were identical with authentic material by melting point, mixture melting point, and nmr and infrared spectra. 3-Hydroxydamsin (**3**) was not detected by nmr or tlc in any fractions from the column.

Synthesis of 3-Hydroxydamsin (3).—Ambrosiol (**6**, 0.5 g, 1.9 mmoles), pyridinium trifluoroacetate (0.1 g), pyridine (0.5 ml), and acetic anhydride (0.3 ml, 3.0 mmoles) were dissolved in 4 ml of dimethyl sulfoxide. After 24 hr at room temperature, the reaction solution was diluted with 25 ml of water and extracted three times with 20-ml portions of chloroform. The combined extracts were dried and concentrated to a syrup. Nmr analysis of the syrup indicated 10% starting material, 13% 3-hydroxydamsin, 64% **7**, and 13% **8**. The mixture was chromatographed over silica gel using first chloroform and later chloroform–ether as eluents. Nmr analysis of the syrups obtained on concentration of the solvent revealed that the first fractions were nearly pure **7**. Later fractions contained mixtures which were mainly **8** and **7**, then **8** and **3**, and finally **3** and **6**. The fractions which contained mostly **3** were combined and rechromatographed over silica gel by eluting with chloroform yielding finally 15 mg of pure crystals which were identical with the natural product by melting point, mixture melting point, infrared, and nmr.

The fractions from the first column which were nearly pure **7** were combined and rechromatographed over silica gel using ether as the eluting solvent. The first cuts afforded a clear, white syrup of **7** (0.1 g), pure by tlc (R_f 0.8 on tlc plates developed in ether) and nmr: ultraviolet (MeOH), λ_{max} 209 mμ ($\epsilon \sim 8000$) and 309 (35); infrared ($CHCl_3$), 3400 (hydroxyl), 1750 (ketone and lactone), and 1650 cm^{-1} (double bond).

Fractions of the first column which contained mostly **8** with a little **7** yielded crystalline **8** on trituration under ether. The crystals which were obtained (20 mg) were sublimed (180°, 0.1 mm of Hg) to give pure **8**: mp 232–233°; ultraviolet (MeOH), λ_{max} 210 mμ (ϵ 9000) and 260 (6600); infrared (Nujol mull), 3200 (hydroxyl), 1700 (conjugated ketone), 1725 (lactone), and 1630 cm^{-1} (double bond).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92; O, 24.40. Found: C, 68.88; H, 6.96; O, 24.19; mol wt (mass spectrum), 262.

Registry No.—**3**, 13250-08-3; **4**, 13250-09-4; **7**, 13250-10-7; **8**, 13250-11-8.

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The Synthesis of Aryl Sulfones

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There are several methods of synthesizing aromatic sulfones, but many of these either give low yields, have serious limitations, or require special techniques.[1]

The most practical laboratory method of preparing aryl sulfones is a Friedel–Crafts method employing a sulfonyl chloride, aromatic hydrocarbon, and aluminum chloride catalyst[2] (eq 1). The yields in this reaction

$$ArSO_2Cl + Ar'H \xrightarrow[AlCl_3]{} ArSO_2Ar' + HCl \qquad (1)$$

are generally satisfactory and range from 60 to 90%.

The oxidation of sulfides and sulfoxides by a variety of oxidizing agents also yields sulfones.[1] The displacement reaction between a sodium sulfinate and an aryl halide gives good yields of aromatic sulfones, but only in the case when strong electron withdrawing groups, such as nitro, are present in the aromatic ring of the halide. Gilman[3] has reported the synthesis of aryl sulfones by the reaction of Grignard reagents with aryl-*p*-toluene sulfinates. The yields vary in this synthesis from 40–80%.

Other preparative methods have involved the removal of water between an aryl sulfonic acid and an aromatic hydrocarbon by some dehydrating agent or at high temperatures as illustrated by reaction 2. Meyer[4]

$$ArSO_3H + Ar'H \xrightarrow[\Delta]{} ArSO_2Ar' + H_2O \qquad (2)$$

prepared several aromatic sulfones by passing the vapor of an aromatic hydrocarbon through a molten solution of a sulfonic acid in the temperature range of 125–200°. The yields in this preparation are low, 30–40%, and often times mixtures of sulfones are obtained through trans-sulfonation reactions. Drews[5] and co-workers found a major complication in this direct condensation reaction which resulted from the desulfonation of the molten sulfonic acid at high temperature. For example, toluene and *p*-xylenesulfonic acid gave not only the expected *p*-tolyl-*p*-xylyl sulfone but also di-*p*-tolyl sulfone and di-*p*-xylyl sulfone. These results cast some doubt on the properties of specific isomers reported in the original work by Meyer,[4] since he was unaware of the above complications.

Another method to effect reaction 2 above has been reported in the early work by Michael and Adair.[6] These investigators used phosphorus pentoxide as the dehydrating agent and obtained sulfones, but only in rather low yields.

In a previous study of the Jacobsen rearrangement of aryl sulfonic acids in polyphosphoric acid,[7] it was observed that sulfones were produced when certain

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(1) For a review of the older methods of preparing sulfones, see C. Suter, "Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, p 658.

(2) H. Beckurts and R. Otto, *Ber.*, **11**, 472, 2066 (1878).

(3) H. Gilman, *et al.*, *J. Am. Chem. Soc.*, **47**, 2047 (1925).

(4) A. Meyer, *Ann.*, **433**, 327 (1923).

(5) H. Drews, S. Meyerson, and E. Fields, *J. Am. Chem. Soc.*, **83**, 3871 (1961).

(6) A. Michael and A. Adair, *Ber.*, **10**, 583 (1877).