## The Acetylation of Thujopsene

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Received June 17, 1971

The acetylation of the hydrocarbon fraction of American cedarwood oil with acetic anhydride-polyphosphoric acid affords two major products, acetylcedrene (2) derived from (-)- $\alpha$ -cedrene and 1-aceto-7,10-ethano-4,4,7-trimethyl-1(9)-octalin (6) derived from (-)-thujopsene (5) by prior isomerization to octalin 8 and subsequent acetylation. The structure of ketone 6 was established by X-ray analysis of the ethylene thioketal derivative.

American cedarwood oil, one of the most economical and abundant sources of sesquiterpenes, is an important oil for the fragrance industry in the United States. The structures of the two best known constituents of this oil,  $\alpha$ -cedrene (1) and cedrol (3), were finally determined by Stork and coworkers<sup>1,2</sup> more than a century after their initial isolation. Subsequent more detailed investigation of the hydrocarbon portion of this oil<sup>3</sup> has shown that in addition to  $\alpha$ -cedrene an almost equal amount (40–50%) of thujopsene (5) is present, along with small amounts (5–15%) of  $\beta$ cedrene (4) and a number of other sesquiterpenes.



Among the numerous derivatives of American cedarwood oil which are utilized in perfumery is a ketonic mixture obtained by the acetylation of the hydrocarbon fractions of this oil with acetic anhydride or acetyl chloride and catalysts such as zinc chloride, aluminum chloride, or boron trifluoride. This product possesses a warm woody odor and is sold under various trade names within the fragrance industry. These findings prompted us to investigate an alternate acetylation procedure employing acetic anhydride with polyphosphoric acid as the catalyst. Under these conditions a product similar to the earlier ketonic mixture but with a greatly enhanced odor value was obtained. No structure elucidations of the components of this mixture have previously been reported and we present here the results of our work in this area.

Acetylation of either pure  $\alpha$ -cedrene (1) or  $\beta$ -cedrene (4) afforded as the sole ketonic product the acetyl derivative 2 which possessed a weak odor of no special interest. Since ketone 2 was identical with the major ketone found in the mixture obtained by acetylation of the hydrocarbon fraction of American cedarwood oil, we suspected that the odor components sought after were instead acetylthujopsene derivatives. Confirmation of this hypothesis was readily obtained by

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acetylation of pure (-)-thujopsene (5) into a mixture of hydrocarbons and ketones containing no acetylcedrene (2) and possessing a strong woody odor.

Analysis of the ketonic portion by gas chromatography revealed the presence of seven major components which were designated in order of elution as isomers A (8%), B (7%), C (3%), D (9%), E (8%), F (13%), and G (52%). Mass spectroscopy showed that each of these components was isomeric and corresponded to a molecular formulation of  $C_{17}H_{26}O$ . These isomers were subsequently obtained in varying degrees of purity via careful spinning-band distillation. In view of the complexity of this mixture we concentrated our initial efforts at structure elucidation on the major (52%) component. This component fortunately possessed a powerful woody-musk-ambergris odor far greater than the other six isomers and could readily be obtained in 95% purity via distillation.

The ir spectrum showed an intense conjugated carbonyl absorption at 1672 cm<sup>-1</sup> and also a strong unusual double bond absorption at 1587 cm<sup>-1</sup>. Elemental analysis and mass spectral data supported a  $C_{17}H_{26}O$  molecular formula which combined with ir data demanded that a tricyclic structure be retained. The nmr spectrum although showing three methyl singlets at  $\delta$  0.78, 0.78, and 0.85 and a methyl ketone singlet at  $\delta$  2.22, clearly had no vinyl hydrogens or vinyl methyl groups and could therefore not be derived from direct acetylation of the thujopsene skeleton. Moreover, although the thujopsene initially charged was optically active, the product ketone was inactive, as were the recovered unacetylated hydrocarbons.

We consequently elected to elucidate unambiguously the structure of the liquid major acetylation product of thujopsene via an X-ray crystal structure determination on a suitable solid derivative. A number of derivatives were prepared and the ethylene thioketal derivative was selected. Proof that this derivative was valid for structure determination was provided by Corey's<sup>4</sup> mild hydrolysis procedure which regenerated a ketone identical with that utilized for the original derivatization. The single crystal X-ray structure analysis showed that the derivative possessed structure 7



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<sup>(1)</sup> G. Stork and R. Breslow, J. Amer. Chem. Soc., 75, 3291 (1953); ibid., 75, 3292 (1953).

<sup>(2)</sup> G. Stork and F. H. Clarke, *ibid.*, **77**, 1072 (1955); *ibid.*, **88**, 3114 (1961).



Figure 1.—Stereodrawing showing the conformation of 7 in the solid state. The ellipsoids represent the thermal motions of each atom at the 50% probability level. The drawing was prepared by a computer program written by C. K. Johnson of the Oak Ridge National Laboratory.

(Figure 1) and the parent ketone must therefore be formulated as 6.

The hydrocarbon mixture which was recovered under the acetylation conditions contained no thujopsene but could be reacetylated to afford the same ketonic mixture as previously obtained directly from thujopsene, implying that isomerization preceded acetylation.



The results of our investigation of the acid-catalyzed isomerization of thujopsene<sup>5</sup> proved that indeed this was true and that the acetylated products arose from this complex mixture of hydrocarbons. Ketone 6 therefore arises by acetylation of the tricyclic olefin 8 formed from thujopsene under the reaction conditions.

Dauben and Friedrich<sup>6</sup> have previously reported the formation of tricyclic hydrocarbon 9 from per-



chloric acid-acetic acid treatment of thujopsene. Treatment of this hydrocarbon under our acetylation conditions afforded a single ketonic product which was found to be identical with the 9% component (isomer D) in the original acetylthujopsene mixture and is thus assigned structure 10.

Ketone 6, the major acetylthujopsene product, appears to be the first known example of a tricyclic compound of this type possessing a strong musk odor. All other known tricyclic musks with an acetyl group<sup>7</sup> also contain an aromatic ring.

## **Experimental Section**

Materials and Equipment.—(-)-Thujopsene (5) was obtained in 99% purity by careful fractional distillation of Hibawood oil through a 2-ft Goodloe column: bp 67-68° (0.5 mm);  $n^{20}$ D 1.5050; [ $\alpha$ ]<sup>26</sup>D -92.5° (neat). (-)- $\alpha$ -Cedrene (1) was obtained in 99% purity by dehydration of (+)-cedrol (3) by the method of Teisseire, et al..<sup>6</sup> bp 64° (0.3 mm);  $n^{20}$ D 1.4978; [ $\alpha$ ]<sup>25</sup>D -88° (neat).

Spectra were recorded on a Perkin-Elmer 457 grating ir spectrophotometer, a Beckman Acta III uv spectrophotometer, a Varian A-60A nmr spectrometer, and a Perkin-Elmer 270 double-focusing mass spectrometer. Spinning-band separations were accomplished with a Nester-Faust NFA-100 autoannular Tefion spinning-band column. Vapor phase chromatography (vpc) was carried out with an F & M 720 equipped with a 2 m  $\times 0.25$  in. copper column packed with 15% Carbowax 20M on Chromosorb P. Combustion analyses were determined by Schwartzkopf Microanalytical Laboratory, Woodside, N. Y.

Acetylcedrene (2).—Acetic anhydride (400 g) was added with cooling to polyphosphoric acid (480 g) with efficient agitation over 10 min. Methylene dichloride (200 ml) was added, followed by (-)- $\alpha$ -cedrene (1, 204 g) with cooling over 10 min, which was agitated at 25° for 2 hr and then at 50° for 3 hr. The mixture was poured onto 1000 g of ice, warmed to 50° for 0.5 hr, and extracted with methylene dichloride. The combined organic extracts were washed with water, sodium carbonate solution, and brine. The solvent was removed at reduced pressure affording 210 g of crude product. This mixture was fractionally distilled affording 66.0 g of recovered  $\alpha$ -cedrene (2), bp 98-105° (0.4 mm), which contained by vpc 81% of the desired component and 19% of five minor components. A pure sample of acetylcedrene (2) was obtained by careful spinning-band distillation: bp 84-86° (0.01 mm);  $n^{50}$ D 1.5152; [ $\alpha$ ]<sup>25</sup>D - 38.5° (neat); ir (neat) 1672 (C=O), 1600 (conj C==C), 1230, 1198, 1160, 1130, 1085, 1020, 970, 935, 640, 600 cm<sup>-1</sup>;  $\delta_{\text{TMS}}^{\text{FDM}}$  2.20 (s, 3), 1.98 (s, 3), 1.02, 0.98 (s, 3 each), 0.90 (d, 3, J = 8 Hz); mass spectrum 246 (11), 161 (36), 119 (20), 69 (20), 43 (100). Anal. Calcd for Ct<sub>17</sub>H<sub>26</sub>O: C, 82.87; H, 10.64. Found: C, 82.78; H, 10.72.

1-Aceto-7,10-ethano-4,4,7-trimethyl-1(9)-octalin (6).—Acetic anhydride (400 g) was added to polyphosphoric acid (480 g) with efficient agitation and cooling over 10 min. Methylene dichloride (200 ml) was added, followed by (-)-thujopsene (5, 204 g) with cooling over 10 min, which was agitated at  $25^{\circ}$  for 2 hr and then at  $50^{\circ}$  for 2 hr. The mixture was poured onto 1000 g of ice, warmed to  $50^{\circ}$  for 0.5 hr, and extracted with methylene dichloride. The combined organic extracts were washed with water, sodium carbonate solution, and brine. The solvent was removed at reduced pressure and the residue was distilled on a still head to afford 171 g of distillate, bp 70-150° (0.2 mm). The distillate was fractionally redistilled affording 63 g of the recovered isomerized hydrocarbon mixture<sup>5</sup> and 104 g (61% based on hydrocarbons consumed) of a ketonic mixture, bp 115-135° (0.2 mm). This ketonic material was comprised of seven components by vpc

<sup>(5)</sup> H. U. Daeniker, A. R. Hochstetler, K. Kaiser, and G. C. Kitchens, *ibid.*, **36**, 1 (1971).

<sup>(6)</sup> W. G. Dauben and L. E. Friedrich, Abstracts of the International Union of Pure and Applied Chemistry, Fifth International Symposium on the Chemistry of Natural Products, London, July 8-13, 1968.

<sup>(7)</sup> T. F. Wood, Givaudanian, Sept (1969); ibid., March-April, (1970).

<sup>(8)</sup> P. Teisseire, M. Plattier, W. Wojnarowski, and G. Ourisson, Bull. Soc. Chim. Fr., 2749 (1966).

and designated as isomers A (8%), B (7%), C (3%), D (9%), E (8%), F (13%), and G (52%) in order of elution. The identical mixture was also formed when the recovered isomerized hydrocarbons<sup>5</sup> were reacetylated under the above conditions. The major component of the ketonic mixture was obtained in pure form by careful spinning-band distillation and exhibited the following properties: bp 92-93° (0.05 mm);  $n^{20}$ D 1.5265; [a]  $^{20}$ D 0.0° (neat);  $\lambda_{\rm max}^{\rm Mc0H}$  257 nm ( $\epsilon$  6750); ir (neat) 1672 (C=O), 1587 (conj C=C), 1247, 1239, 1175, 940 cm<sup>-1</sup>;  $\delta_{\rm TMS}^{\rm CDCI3}$  2.21 (s, 3), 0.85 (s, 3), 0.79 (s, 6); mass spectrum 246 (43), 218 (31), 203 (58), 161 (32), 43 (100), 41 (36).

Anal. Calcd for  $C_{17}H_{26}O$ : C, 82.87; H, 10.64. Found: C, 82.79; H, 10.71.

Ethylene Thioketal Derivative of 1-Aceto-7,10-ethano-4,4,7trimethyl-1(9)-octalin (7).—A sample of ketone 8 (1.0 g), acetic acid (10 ml), ethanedithiol (1.1 ml), and boron trifluoride etherate (1.1 ml) was allowed to stand at 25° for 3.5 hr. Water (50 ml) was added and the mixture was extracted with hexane. The organic phase was washed with water, 5% aqueous NaOH, and water and dried (MgSO<sub>4</sub>). The solvent was removed and the residue crystallized from hexane to afford 950 mg (72%) of thioketal 7: mp 74-75°; ir (KBr) 1279, 1142, 1129, 1035, 1019, 853 cm<sup>-1</sup>;  $\delta_{\text{TMS}}^{\text{CDCls}}$  3.28 (s, 4), 1.90 (s, 3), 0.88 (s, 3), 0.77 (s, 6); mass spectrum 322 (2), 261 (100), 232 (24), 217 (30), 175 (25), 106 (27), 59 (28). An additional slow recrystallization from hexane afforded crystals suitable for an X-ray crystal structure determination, mp 76-77°.

Anal. Calcd for  $C_{10}H_{30}S_2$ : C, 70.72; H, 9.38; S, 19.89. Found: C, 70.91; H, 9.17; S, 20.08. Hydrolysis of Thioketal 7.—The procedure of Corey and Crouse

Hydrolysis of Thioketal 7.—The procedure of Corey and Crouse was employed.<sup>4</sup> A mixture of thioketal 7 (75 mg), acetonitrile (2.3 ml), water (0.12 ml), HgCl<sub>2</sub> (134 mg), and CdCO<sub>3</sub> (88 mg) was stirred under N<sub>2</sub> at 50° for 6.5 hr. The mixture was then evaporated to dryness, benzene added, and the mixture filtered. The benzene solvent was removed affording 45 mg of yellow oil. The ir, nmr, and mass spectra were identical with those of ketone 8, the major product from the acetylation of thujopsene, from which the thioketal derivative 7 had been prepared.

4-Aceto-2,2,3,7-tetramethyltricyclo[ $5.2.2.0^{1,6}$ ]undec-3-ene (10).—The procedure previously outlined for the preparation of ketone 6 was employed with olefin 9 (10.0 g), acetic anhydride (19.6 g), and polyphosphoric acid (23.5 g). After the same work-up procedure the residue was distilled affording 4.8 g of recovered olefin 9 and 5.4 g of desired ketone product, bp 132–135° (0.5 mm). A sample of the major (70%) ketonic product was isolated by preparative vpc and exhibited the following properties:  $n^{20}$ p 1.5155; ir (neat) 1690 (C=O), 1615 (conj C=C), 1240, 1225, 1205 cm<sup>-1</sup>;  $\delta_{100}^{CDCl_8}$  2.33 (s, 3), 1.72 (s, 3), 1.03 (s, 3), 1.00 (s, 3), 0.93 (s, 3); mass spectrum 246 (16), 231 (35), 203 (25), 133 (17), 119 (17), 95 (15), 43 (100). The spectral properties were identical with those of isomer D isolated from the acetylation of thujopsene by the above procedure.

Anal. Calcd for C<sub>17</sub>H<sub>28</sub>O: C, 82.87; H, 10.64. Found: C, 82.90; H, 10.57.

**X-Ray Analysis of 7.**—The ethylene thioketal derivative 7 crystallizes as well-formed prisms from hexane. The crystal data are a = 11.530 (8), b = 9.246 (6), c = 16.873 Å (10),  $\beta = 92.08$  (6)°, space group  $P2_1/a$ ,  $d_{obsd} = 1.19$  g cm<sup>-3</sup> (flotation in aqueous KI),  $d_{ealed} = 1.19$  g cm<sup>-3</sup> for Z = 4. The intensity data were measured by a moving crystal-moving detector method on a Hilger-Watts Model Y290 four-circle diffractometer. Nickel filtered Cu K $\alpha$  radiation and pulse height discrimination were used. A total of 3586 independent reflections were measured ( $2\theta < 140^{\circ}$ ) of which 2345 were unobservably weak and were not included in the structure analysis. The crystal used for data collection was approximately 0.12  $\times$  0.15  $\times$  0.22 mm. The function minimized in the least-squares refinement was  $\Sigma w ||F_0| - |F_0||^2$  where  $w = 1/(11.8 + |F_0| + 0.012|F_0|^2)$ . Standard atomic scattering curves were used for S, C, <sup>9</sup> and H.<sup>10</sup> The refinement calculations were made with a local modification of the program ORFLS.<sup>11</sup>

The structure of 7 was solved by the heavy atom method. A difference Fourier calculated after three cycles of full matrix least squares (anisotropic temperature factors for all atoms) clearly showed all the hydrogen atoms. Refinement was continued by block diagonal least squares ( $9 \times 9$  blocks for the anisotropic atoms,  $4 \times 4$  blocks for the hydrogen atoms) until the shifts in all parameters of the heavier atoms were less than  $\frac{1}{4}$  of their standard deviations ( $\frac{1}{2}$  of a standard deviation for the hydrogens). A difference Fourier based on the final parameters showed no features greater than  $0.15 \text{ e} \text{ Å}^{-2}$  in magnitude. The final conventional unweighted R factor is 5.1%.<sup>12</sup>

**Registry No.**—2, 32388-55-9; 5, 470-40-6; 6, 32388-56-0; 7, 32388-57-1; 10, 32388-58-2.

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(12) Listings of structure factors, coordinates, and thermal parameters for 7 will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Reprint Department, ACS Publications, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to author, title of article, volume, and page number. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche.