Chemistry of Resin Acids. I. The Reaction of Levopimaric Acid with Formaldehyde

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Levopimaric acid reacted with formaldehyde to form a Diels–Alder-type adduct in high yield. The ether linkage of the adduct was ruptured under acid conditions to give 6-hydroxymethylabietic acid. 6-Hydroxymethylabietinol was prepared by reduction and rearrangement of the adduct or by reduction of the hydroxy acid.

Since the development of a convenient means for the isolation of pure levopimaric acid,[2] the chemistry of this compound has been of continuing interest in this laboratory. During the course of our work on the methylolation of resin acid mixtures high in levopimaric acid content, our attention turned to the investigation of the reaction of pure levopimaric acid with formaldehyde.

Upon heating levopimaric acid (I) with formaldehyde under conditions similar to those used for resin acid mixtures,[3] a hydroxy acid was obtained which gave an ultraviolet absorption spectrum almost identical in form with that of abietic acid but with a principal maximum at 243 instead of 241 mμ. Rearrangement to an abietic-type double-bond system had apparently taken place. Substitution of the methylol group on a carbon of the conjugated double-bond system of abietic acid should, according to Woodward rules, have given a shift of the ultraviolet maximum to 246 mμ. Such a shift was observed by Royals and Greene[4] as a result of the Prins reaction on abietic acid. By careful control of the reaction conditions and the conditions of product isolation, a crystalline intermediate was isolated which showed no ultraviolet absorption above 210 mμ and contained no free hydroxyl group. This product was subsequently shown to be the cyclic ether II resulting from the Diels–Alder-type addition of formaldehyde to levopimaric acid. The purified adduct was somewhat unstable, being converted to 6-hydroxymethylabietic acid III on heating or by treatment at room temperature with dilute mineral acids. This was identical with the hydroxy acid obtained directly from levopimaric acid under more stringent reaction conditions. Hydrogenation of the adduct took place readily over Pd–C (5%) catalyst with the absorption of more than 1 mole of hydrogen. Free hydroxyl absorption bands in the infrared spectra of the gross product indicated partial opening of the adduct and thereby accounted for the excessive absorption of hydrogen. Fractional crystallization gave a high-melting solid showing no free hydroxyl absorption in the infrared spectrum and giving a n.m.r. spectrum with the expected changes for the hydrogenated adduct. Reduction of the carboxylic acid function of the adduct with lithium aluminum hydride followed by acid hydrolysis of the mixture gave the ether-insoluble diol IV. The diol was further converted to its diacetate for purposes of analysis.

Alkaline hydrolysis of the $LiAlH_4$ reduction mixture allowed the isolation of a monohydroxylic material V which was readily converted to the diol IV upon treatment with dilute HCl.

The only known *cis*-diene structures which could be involved, and which are thereby capable of giving the Diels–Alder addition[5] observed, are those of levopimaric acid and palustric acid (the 4b–8a, 7–8 dienoic acid). The involvement of palustric acid seems unlikely in view of the speed and temperature at which the addition proceeds as compared to the thermal conversion of levopimaric to palustric acid.[6]

The n.m.r. spectra of the adduct II and the hydrogenated adduct were run in pyridine solution using tetramethylsilane as an internal standard. The following peak assignments were made. A one-proton peak (somewhat broadened) at δ 5.79 is attributed to the C-8 vinyl proton. A pair of doublets centered at δ 3.78 and 3.19, respectively, having $J = 7 \pm 0.2$ c.p.s. is an AB pattern attributed to geminal coupling of the oxygen-bearing methylene protons. These doublets show further splitting ($J = 1.5$ c.p.s.) but the patterns are not well defined. Coupling with the C-6 proton is apparently quite weak. A three-proton peak at δ 1.35 is assigned to the C-1 angular methyl protons. A six-proton doublet at δ 1.07 is assigned to the methyl protons of the isopropyl group and a three-proton peak at δ 0.54 is assigned to the C-4a angular methyl protons. The remainder of the spectrum consisted of rather broad peaks between δ 1.3 and 2.6.

The spectrum of the hydrogenated adduct showed the expected disappearance of the vinyl proton absorption at δ 5.79. In addition the six-proton doublet had shifted upfield and the three-proton 4a methyl signal had shifted downfield to coincide at δ 0.91. The C-1 methyl proton signal remained about the same at δ 1.35. The doublet of the oxygen-bearing methylene proton *endo* to the original double bond had shifted downfield and the somewhat broadened doublets of the AB system were centered at δ 4.01 and 3.78.

These spectra are readily rationalized on the basis of addition of the formaldehyde to the back side of the levopimaric acid molecule to place the double bond in a position to strongly shield the C-4a methyl group. The same shielding effect has been reported for the maleic anhydride adduct.[7] Since there are only two protons indicated in the region δ 4–3, the oxygen must

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(2) H. B. Summers, Jr., W. D. Lloyd, and G. W. Hedrick, *Ind. Eng. Chem., Prod. Res. Develop.*, **2**, 173 (1963).

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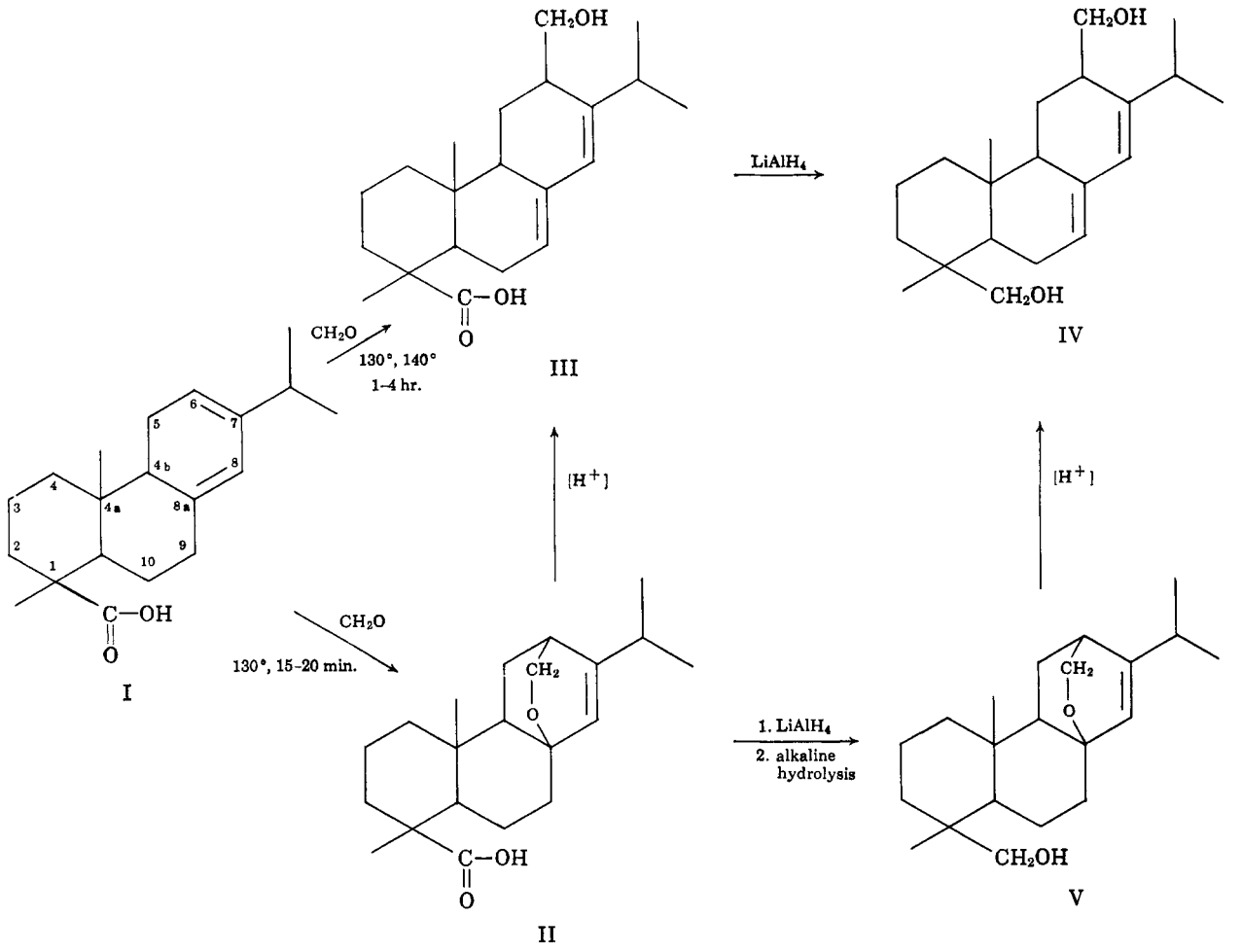
(7) W. A. Ayer, C. E. McDonald, and J. B. Stothers, *Can. J. Chem.*, **41**, 1113 (1963).



be bonded to a tertiary carbon. The proposed adduct structure would result in a 6-α-methylolabietic acid on opening of the ether ring. As has already been pointed out, this structure is consistent with the ultraviolet absorption spectrum which indicates that the added group is not situated on a carbon of the conjugated diene system. The shape and strength of the ultraviolet absorption curve also indicates a structure very similar to that of abietic acid.

Diels–Alder-type addition reactions involving formaldehyde as the dienophile have been observed before[8] but in no previous instance has the ease of product formation observed with levopimaric acid been noted.

The levopimaric acid–formaldehyde adduct has been prepared directly from pine gum having as little as 37% levopimaric acid content in the resin acids. The adduct has been converted to its methyl ester and sodium reduction of the ester with acid treatment has yielded a crystalline diol. These reactions should offer an economical route to a pure, high molecular weight diol from pine gum and are currently the subject for further study on this material.

Experimental

The Reaction of Levopimaric Acid with Formaldehyde.—Levopimaric acid (30 g., 0.1 mole) was placed in a flask with paraformaldehyde (6.6 g., 0.22 mole) and stirred with a paddle-type stirrer while heating in an oil bath at 140°. After 50 min., dioxane (75 ml.) was added to solubilize the materials and the mixture was heated at reflux for about 2 hr. The mixture was cooled, diluted with ether, and washed with water. The ether solution was shaken with sodium sulfate, filtered, and evaporated to a light-colored friable resin.

Anal. Calcd. for $C_{21}H_{32}O_3$: neut. equiv., 332; active H equiv. (HaE, grams of sample required to evolve 1 mole of hydrogen on treatment with excess lithium aluminum hydride), 166. Found: neut. equiv., 308; HaE, 194.3.

A 5-g. sample of the material was treated with excess $LiAlH_4$ in ether and allowed to stand overnight. The mixture was hydrolyzed with excess, dilute, iced hydrochloric acid and the ether solution was washed chloride free with water. The ether solution was dried over Na_2SO_4, filtered, and concentrated. A product (III) having $\lambda_{max}^{ethanol}$ 243 mμ (ϵ 23,620), $[\alpha]^{27}D$ −73.7°, m.p. 179.5–181.3°, was isolated.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; HaE, 158. Found: C, 79.24; H, 10.63; HaE, 170.

The diol was converted to the diacetate by either refluxing with excess acetic anhydride or by treatment of a pyridine solution of the diol with a slight excess of acetyl chloride. The diacetate was molecularly distilled at 135° (20 μ). The product was a very viscous, water-white liquid, $[\alpha]^{27}D$ −47.76°.

Anal. Calcd. for $C_{25}H_{38}O_4$: C, 74.55; H, 9.51; sapon. equiv., 201.3. Found: C, 74.5; H, 9.47; sapon. equiv., 202.

The Diels–Alder Adduct of Levopimaric Acid and Formaldehyde.—Levopimaric acid (60 g., 95% purity, 0.18 mole) and paraformaldehyde (9 g., 0.3 mole) were placed in a 200-ml. flask equipped with a paddle-type stirrer and heated in an oil bath held at 130°. The mixture was stirred for about 8 min. and the temperature was raised to 135°. The mixture began to fuse and after another 12–15 min. it had passed through a semisolid slush stage and resolidified. Ether (100 ml.) and water (50 ml.) were introduced and the solid lumps were broken up. The mixture was filtered; the ether filtrate was separated and concentrated to yield crystalline II (4.6 g.). This and the dried cake (41.9 g.) gave a total yield of 70.6% (46.5 g.). The final ether filtrate was evaporated to a pale yellow resin (16.2 g.) which had λ_{max} at 243 mμ (α 41), indicating about 55% of the residue to be 6-methylolabietic acid [$\lambda_{max}^{ethanol}$ 243 mμ (ϵ 24,290)]. The crystalline adduct was recrystallized from methanol, m.p. 162.5–163.5°, $[\alpha]^{27}D$ +82.0°.

(8) T. L. Gresham and T. R. Steadman, *J. Am. Chem. Soc.*, **71**, 737 (1949).

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.69; H, 9.72.

Hydrogenation of Levopimaric Acid–Formaldehyde Adduct.—The recrystallized adduct (15 g.) was placed in a low-pressure hydrogenator with ethanol (75 ml.) and 5% palladium-on-carbon catalyst (0.75 g., 5%). Hydrogenation was allowed to proceed overnight at 40–45 p.s.i.g. All of the adduct had dissolved. The mixture was filtered and the product was precipitated by addition of water. A semicrystalline material was obtained. The infrared spectra showed free hydroxyl bands indicating at least a partial opening of the cyclic ether. The material was redissolved in a minimum of 95% ethanol and allowed to stand overnight. A crystalline solid precipitated (3 g., 20%), m.p. 240.9–243.8°, $[\alpha]^{27}D$ +106.5°. No other pure crystalline product was isolated.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25; neut. equiv., 334.49. Found: C, 75.70; H, 10.25; neut. equiv., 337.8.

A quantitative hydrogenation gave a hydrogenation equivalent of 286 (calcd. for $C_{21}H_{32}O_3$, 332). The low value may be a result of partial hydrogenation of the second double bond of the hydroxy acid formed during hydrogenation.

Conversion of Adduct II to the Hydroxy Ether V.—Recrystallized adduct (10 g.) was slurried in dry ether (50 ml.) and added to an ether solution of $LiAlH_4$ (3 g. in 50 ml.) with rapid stirring. The mixture stood 4 hr. at room temperature and was then hydrolyzed by cautious dropwise addition of 6 *N* NaOH until the solids clumped to a granular mass. The mixture was filtered; the ether solution of the product was concentrated by evaporation and filtered to yield crystalline V (6.1 g., 60%), m.p. 124–126°, $[\alpha]^{27}D$ +94.8°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.08; H, 10.64.

A small sample of the hydroxy ether was dissolved in 3 vol. of ether and shaken with 1 drop of dilute (3 *N*) HCl. After about 3 min. crystalline diol precipitated. A mixture melting point with good diol showed no depression.

Conversion of the Levopimaric Acid–Formaldehyde Adduct to 6-Methylolabietic Acid.—Recrystallized adduct (33 g., 0.1 mole) was dissolved in 50–75 ml. of ethanol (95%) and 6 *N* hydrochloric acid (5 ml.) was added. The solution, after standing 15 hr. at room temperature, was diluted with water until no further precipitation occurred. The oil which separated crystallized on standing. The solids (29.9 g.) were taken up in methanol (25 ml.), heated to the boiling point while adding water to the cloud point, seeded with crystalline hydroxy acid, and set aside to crystallize. The mixture was further cooled in the refrigerator and then filtered; the solid was (III) dried in a vacuum desiccator (27.3 g., 83.2% yield), m.p. 166.5–168°, $[\alpha]^{23.8}D$ 48.2°, $\lambda_{max}^{ethanol}$ 243 mμ (ε 24,290).

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.71; neut. equiv., 332.47. Found: C, 75.86; H, 9.70; neut. equiv., 334.0.

The hydroxy acid was reduced with excess $LiAlH_4$ in ether to the diol. The mixture melting point showed no depression with the diol from the $LiAlH_4$ reduction of the resinous product obtained on longer heating of levopimaric acid and formaldehyde or that obtained from reduction of the crystalline adduct followed by acid hydrolysis.

Levopimaric Acid–Formaldehyde Adduct from Pine Gum.—Pine gum (1000 g.) containing 18.5% levopimaric acid was placed in a stirred resin reactor with paraformaldehyde (150 g.). The mixture was stirred and heated to reflux (120°) where it was maintained for about 20 min. The material was poured slowly into diethyl ether (1 l.), filtered, and allowed to stand and crystallize. The mixture was then chilled to near 0° and filtered to yield crude adduct II, 120 g. (58%).

Methyl Ester of Levopimaric Acid–Formaldehyde Adduct.—Purified levopimaric acid–formaldehyde adduct (111 g.) was dissolved in dioxane (500 ml.) and placed in a resin reactor with *n*-hexane (100 ml.). The solution was stirred rapidly and a solution of sodium hydroxide (15 g.) in water (20 ml.) was added. The mixture was stirred and heated to distil the *n*-hexane–water azeotrope. The water was collected until it ceased to be evolved. The dried salt–solvent mixture was cooled and transferred to a rocking autoclave with methyl chloride (49 g.). The mixture was rocked and heated at 150° for 20 hr. After cooling, the charge was removed from the bomb and the ester was precipitated by dilution with water. The ester was taken up in ether, washed with alkali to remove any unreacted acid, and dried over anhydrous sodium sulfate. Filtration and evaporation of the ether gave 74 g. (64%) of viscous liquid ester, $[\alpha]^{27}D$ +74.4°.

Sodium Reduction of Adduct Methyl Ester.—Crude adduct methyl ester (16 g., 0.05 mole) was dissolved in *t*-butyl alcohol (20 g., 0.262 mole) and xylene (20 ml.). The solution was added rapidly to a violently agitated mixture of sodium (6 g., 0.262 mole) and xylene (25 ml.) heated to reflux. Solids precipitated during the run. Xylene (65 ml.) was added to promote mixing. The mixture was heated to reflux for 20 min. after addition had been completed. Water was added slowly to hydrolyze the mixture and the mixture was extracted with ether. The ether solution was washed alkali free with water, dried over sodium sulfate, filtered, and evaporated to a resinous product. The product was redissolved in ether, shaken with 5 ml. of 6 *N* HCl, and allowed to stand. Solid precipitated and was removed by filtration, m.p. 175–178°. No melting point depression was observed on mixing with known diol. The crude crystalline diol was recovered in 30% yield.

All melting points were taken in a stirred liquid bath and are uncorrected. Optical rotations were run in 95% ethanol at 2% concentration except for the diol which was run at 1% owing to limited solubility.

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