[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

Reactions of Vanillin and Its Derived Compounds. XXVI.[1] The Synthesis of Propenylvanillil Derivatives[2]

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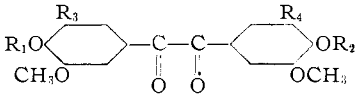
5-Propenylvanillil and 5,5'-dipropenylvanillil were synthesized from vanillil *via* the Claisen rearrangement of the mono- and diallyl ethers of vanillil. The resulting 5-allylvanillil and 5,5'-diallylvanillil were again rearranged to the desired propenyl compounds. 5,5'-Dipropenylvanillil also was prepared by benzoin condensation of 5-propenylvanillin benzyl ether and oxidation of the intermediate 5,5'-dipropenylvanilloin bis-benzyl ether to 5,5'-dipropenylvanillil. The latter compound was debenzylated by means of acetic anhydride and perchloric acid to the desired diacetate of 5,5'-dipropenylvanillil. The last compound was obtained in the three possible forms, namely, *cis–cis*, *trans–trans* and *cis–trans*.

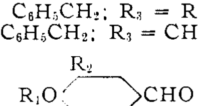
A few years ago[3] the possibility of the presence in at least a part of the complex lignin structure of a linkage between the α-carbon atoms of two C_6–C_3 units was suggested. More recently, it was demonstrated that except for the compounds having carbon chains in the 5-position of the guaiacyl group, the compounds formed in alkaline cupric oxide oxidations of lignosulfonate materials actually could be prepared by similar oxidation of bis-vanillyl compounds such as vanillil and its reduction products.[4] It was next desired to submit bis-vanillyl compounds possessing carbon side chains in the 5-position to the alkaline cupric oxide oxidation process to determine whether such model substances would yield the same products of oxidation as do the lignosulfonate materials. Furthermore, it was hoped to develop good synthetic procedures for the preparation of some of the compounds previously obtained only in small quantities from the lignosulfonate oxidations. The present paper reports the preparation of a number of bis-vanillyl model compounds possessing carbon chains in the 5-position comprising mono- and disubstituted allyl- and propenylvanillils. These substituted vanillils will be employed as model compounds for lignosulfonate oxidation studies.

Vanillil (I) was allylated to its monoallyl ether (II) and diallyl ether (III). These two ethers were rearranged to 5-allylvanillil (IV) and 5,5'-diallylvanillil (V), respectively, by heating in boiling diethylaniline. The last two compounds again were rearranged by caustic fusion in methanol to yield 5-propenylvanillil (VI) and 5,5'-dipropenylvanillil (VII), respectively. All phenolic compounds were characterized by acetates. Acetylation of VII with acetic anhydride in pyridine yielded two of the three possible isomers of 5,5'-dipropenylvanillil diacetate (XII).

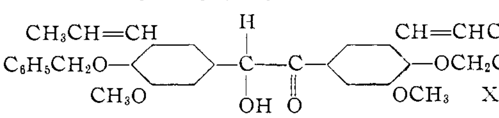
The synthesis of VI and VII also was attempted by another route. 5-Propenylvanillin (XIII) was benzylated to O-benzyl-5-propenylvanillin (XIV) which was then subjected to the benzoin condensation. The intermediate 5,5'-dipropenylvanilloin bis-benzyl ether (XV) which was obtained as a resinous solid was oxidized directly to 5,5'-dipropenylvanillil bis-benzyl ether (XVI). The latter compound was debenzylated with acetic anhydride and perchloric acid to yield XII with a different melting point than the two isomers isolated above. Thus, all three possible isomers of XII were isolated. No further work on the stereochemistry of XII was performed and the structures for the *cis–cis*, *cis–trans* and *trans–trans* isomers have not been assigned. Mixed benzoin condensation of XIII with O-benzylvanillin (XVII) gave a mixture which was oxidized directly to a mixture of vanillil bis-benzyl ether (XVIII), 5-propenylvanillil bis-benzyl ether and XVI. This latter mixture could not be resolved by crystallization, so it was debenzylated with acetic anhydride and perchloric acid, and the mixture of acetates hydrolyzed with ethanolic potassium hydroxide. The mixture of phenolic materials was spotted on paper along with authentic samples of I, VI and VII. Spots for all three compounds were found in the mixture along with three unidentified spots, presumably the intermediate benzoins. No attempt was made to isolate VI and VII from this mixture.



I, $R_1 = R_2 = R_3 = R_4 = H$
II, $R_1 = CH_2{=}CHCH_2{-}$; $R_2 = R_3 = R_4 = H$
III, $R_1 = R_2 = CH_2{=}CHCH_2{-}$; $R_3 = R_4 = H$
IV, $R_1 = R_2 = R_4 = H$; $R_3 = CH_2{=}CHCH_2{-}$
V, $R_1 = R_2 = H$; $R_3 = R_4 = CH_2{=}CHCH_2{-}$
VI, $R_1 = R_2 = R_4 = H$; $R_3 = CH_3CH{=}CH{-}$
VII, $R_1 = R_2 = H$; $R_3 = R_4 = CH_3CH{=}CH{-}$
VIII, $R_1 = CH_2{=}CHCH_2{-}$; $R_2 = CH_3CO$; $R_3 = R_4 = H$
IX, $R_1 = R_2 = CH_3CO$; $R_3 = CH_2{=}CHCH_2{-}$; $R_4 = H$
X, $R_1 = R_2 = CH_3CO$; $R_3 = R_4 = CH_2{=}CHCH_2{-}$
XI, $R_1 = R_2 = CH_3CO$; $R_3 = CH_3CH{=}CH{-}$; $R_4 = H$
XII, $R_1 = R_2 = CH_3CO$; $R_3 = R_4 = CH_3CH{=}CH{-}$
XVI, $R_1 = R_2 = C_6H_5CH_2$; $R_3 = R_4 = CH_3CH{=}CH{-}$
XVIII, $R_1 = R_2 = C_6H_5CH_2$; $R_3 = R_4 = H$
XIX, $R_1 = R_2 = C_6H_5CH_2$; $R_3 = CH_3CH{=}CH{-}$; $R_4 = H$



XIII, $R_1 = H$; $R_2 = CH_3CH{=}CH{-}$
XIV, $R_1 = C_6H_5CH_2$; $R_2 = CH_3CH{=}CH{-}$
XVII, $R_1 = C_6H_5CH_2$; $R_2 = H$



XV

Experimental

All melting points are uncorrected, ultraviolet spectral data are for solutions in 95% ethanol (concentration, 0.02 g. per liter), and R_f values are given for the system butanol–2% aqueous ammonia at 20°.

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[1] For paper XXV of this series, see THIS JOURNAL, **77**, in press (1955).

[2] Presented before the Division of Organic Chemistry at the 127th Meeting of the American Chemical Society, Cincinnati, Ohio, March 29 to April 7, 1955.

[3] I. A. Pearl and E. E. Dickey, THIS JOURNAL, **74**, 614 (1952).

[4] I. A. Pearl and D. L. Beyer, *ibid.*, **76**, 2224 (1954).

Allylation of Vanillil.—A mixture of 151 g. (0.5 mole) of vanillil and 700 cc. of 95% ethanol was treated with 37 g. (0.56 mole) of 85% potassium hydroxide under reflux with silicone oil-sealed stirring. With continued stirring, the mixture was heated to boiling and treated with 67 g. (0.55 mole) of allyl bromide through the reflux condenser. Boiling and stirring under reflux were continued, and after four hours the reflux condenser was placed in the distilling position. When the volume of the reaction mixture was reduced one-half, the residue was diluted to 3 liters with water, basified with potassium hydroxide and filtered. The crystalline precipitate was washed first with dilute potassium hydroxide and then with water and dried to yield 77 g. of III as almost colorless needles melting at 157–158°. Recrystallization from either ethanol or acetic acid yielded silky needles melting at 158–159°. The ultraviolet absorption spectrum showed the following maxima: $\lambda_{\max.}$ 230 mμ, ϵ 22840; $\lambda_{\max.}$ 285 mμ, ϵ 18700: $\lambda_{\max.}$ 322 mμ, ϵ 19700.

Anal. Calcd. for $C_{22}H_{22}O_6$: C, 69.10; H, 5.80. Found: C. 68.98; H, 5.84.

The alkaline filtrate and washings were acidified dropwise with vigorous stirring with acetic acid. A yellow precipitate separated. Acidification was stopped when a trace of white precipitate appeared. At this point the *p*H was approximately 8.0. The yellow precipitate was filtered, washed with water and air-dried to yield 60 g. of II melting at 114–117°. Recrystallization from ether gave yellow crystals melting at 119–120°. The R_f was 0.60 and the ultraviolet absorption spectrum showed the maxima: $\lambda_{\max.}$ 230 mμ, ϵ 21840; $\lambda_{\max.}$ 285 mμ, ϵ 17100; $\lambda_{\max.}$ 320 mμ, ϵ 19480.

Anal. Calcd. for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found: C, 66.70; H, 5.43.

Acetylation of II with acetic anhydride in pyridine and recrystallization of the product from methanol yielded yellow crystals of vanillil monoallyl ether acetate (VIII), melting at 135–136° and having an ultraviolet absorption spectrum with the maxima: $\lambda_{\max.}$ 224 mμ, ϵ 26590; $\lambda_{\max.}$ 277 mμ, ϵ 15390; $\lambda_{\max.}$ 320 mμ, ϵ 14120.

Anal. Calcd. for $C_{21}H_{20}O_7$: C, 65.61; H, 5.24. Found: C, 65.68; H, 5.27.

Further acidification of the original aqueous solution yielded vanillil which could be used in successive experiments.

5-Allylvanillil (IV).—A suspension of 39 g. of II in 200 cc. of diethylaniline was heated to boiling under reflux for 8 hours and allowed to cool. The resulting solution was stirred into 3 liters of a mixture of dilute sulfuric acid and ice. The tan precipitate was filtered, washed with dilute sulfuric acid and then with water, and allowed to air dry. The dry product was covered with acetic acid, and after a short while the dark solution deposited white crystals. After standing overnight, the mixture was filtered, and the white crystals were washed first with acetic acid and then with ether to yield 23 g. of IV melting at 178–179°. The R_f was 0.50 and the ultraviolet absorption spectrum showed the maxima: $\lambda_{\max.}$ 230 mμ, ϵ 22990; $\lambda_{\max.}$ 322 mμ, ϵ 19900. Thus, the 285 mμ maximum disappeared upon rearrangement of the allyl group from the oxygen to the 5-carbon.

Anal. Calcd. for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found: C, 66.62; H, 5.37.

Acetylation of IV with acetic anhydride in pyridine and recrystallization of the product twice from ethanol yielded light yellow crystals of 5-allylvanillil diacetate (IX), melting at 134–135° and giving the following ultraviolet absorption maxima: $\lambda_{\max.}$ 267 mμ, ϵ 10480; $\lambda_{\max.}$ 322 mμ, ϵ 4380.

Anal. Calcd. for $C_{23}H_{22}O_8$: C, 64.78; H, 5.20. Found: C. 64.72; H, 5.24.

5,5′-Diallylvanillil (V).—This compound was obtained by heating III in diethylaniline in the same manner. The crude product obtained from the acetic acid solution was recrystallized from ether to yield very light yellow crystals of the hemihydrate of V melting at 125–126° with gas evolution. The yield was 22 g. although more could be obtained by work-up of the acetic acid filtrate. The R_f was 0.73 and the ultraviolet absorption spectrum showed the maxima: $\lambda_{\max.}$ 230 mμ, ϵ 25090; $\lambda_{\max.}$ 324 mμ, ϵ 20550.

Anal. Calcd. for $C_{22}H_{23}O_{6.5}$: C, 67.50; H, 5.92. Found: C, 67.47; H, 5.98.

Acetylation of V in the usual manner and recrystallization from ethanol yielded light yellow crystals of its diacetate X, melting at 193–194° and giving an absorption spectrum with no maximum, but with a continual rise from higher to lower wave lengths.

Anal. Calcd. for $C_{26}H_{26}O_8$: C, 66.94; H, 5.62. Found: C, 66.96; H, 5.62.

5-Propenylvanillil (VI).—A hot solution of 60 g. of 85% potassium hydroxide in 75 cc. of methanol was treated with 22 g. of IV. The dark solution was boiled under reflux with occasional shaking for 6 hours. The reaction mixture was diluted with 250 cc. of water and poured with stirring into a mixture of 150 cc. of acetic acid and 350 cc. of water. A resinous yellow precipitate separated. After standing overnight the precipitate was filtered, washed with water, sucked as dry as possible and covered with cold methanol. By this treatment the resinous solid was transformed to a yellow powder which melted at 89°, resolidified and melted again at 165–167°. The R_f was 0.40. Recrystallization from ethanol yielded 16 g. of yellow crystals of 5-propenylvanillil hemihydrate melting at 169–170° and having an R_f of 0.40. The ultraviolet absorption spectrum showed the maxima: $\lambda_{\max.}$ 240 mμ, ϵ 2360; $\lambda_{\max.}$ 325 mμ, ϵ 18500.

Anal. Calcd. for $C_{19}H_{19}O_{6.5}$: C, 64.95; H, 5.45. Found: C, 64.86; H, 5.99.

Acetylation of VI in the usual manner and recrystallization twice from ethanol yielded light yellow crystals of its diacetate XI melting at 152–153°. The ultraviolet absorption spectrum indicates a gradual rise in absorption from higher to lower wave lengths with a break in the curve at 315 mμ.

Anal. Calcd. for $C_{23}H_{22}O_8$: C, 64.78; H, 5.20. Found: C, 64.66; H, 5.19.

5,5′-Dipropenylvanillil (VII).—This compound was prepared from 20 g. of V in a manner almost identical with that outlined for the preparation of VI. The yield was 14.5 g. of product melting at 166–169°. Recrystallization from dilute methanol in the presence of decolorizing carbon gave light yellow crystals of VII melting at 176–177°. The R_f was 0.75 and the ultraviolet absorption spectrum showed the maxima: $\lambda_{\max.}$ 250 mμ, ϵ 38220; $\lambda_{\max.}$ 333 mμ, ϵ 19740.

Anal. Calcd. for $C_{22}H_{22}O_6$: C, 69.10; H, 5.80. Found: C, 69.06; H, 5.85.

The methanolic filtrate from the last crystallization was diluted with water to give a tarry precipitate which could not be crystallized. Acetylation of the tarry precipitate in the usual manner and recrystallization from ethanol yielded XII melting at 154–155° and having the maxima in its ultraviolet absorption spectrum: $\lambda_{\max.}$ 228 mμ. ϵ 33200; $\lambda_{\max.}$ 287 mμ, ϵ 12780.

Anal. Calcd. for $C_{26}H_{26}O_8$: C, 66.94; H, 5.62. Found: C, 66.94; H, 5.74.

Acetylation of the 176–177° melting crystals of VII and recrystallization from acetic acid yielded crystals of XII melting at 219–220° and having an ultraviolet absorption spectrum almost identical with that of the 154–155° melting isomer.

Anal. Calcd. for $C_{26}H_{26}O_8$: C, 66.94; H, 5.62. Found: C, 66.92; H, 5.71.

O-**Benzyl-5-propenylvanillin (XIV).**—A mixture of 66 g. (0.5 mole) of 85% potassium hydroxide pellets and 500 cc. of 95% ethanol was stirred under reflux and treated first with 96 g. (0.5 mole) of *trans*-XIII[5] and then with 67 g. (0.53 mole) of benzyl chloride. The reaction mixture was heated to boiling with stirring under reflux for 5 hours, concentrated to approximately 400 cc., and diluted with 3 liters of water. The mixture was extracted with ether and the ether was dried and distilled to yield 145 g. of yellow oil. The oil was distilled under reduced pressure to yield 110 g. of XIV as a light yellow oil boiling at 186° at 1.0 mm. and having $n^{25}\text{D}$ 1.5901. The ultraviolet absorption spectrum indicated a maximum, $\lambda_{\max.}$ 275 mμ, ϵ 10710.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.56; H, 6.51.

A similar experiment with *cis*-XIII yielded the same product.

5,5′-Dipropenylvanillil Bis-benzyl Ether (XVI).—A solution of 30 g. of XIV in 40 cc. of ethanol was treated with a solution of 6 g. of potassium cyanide in 25 cc. of water, and the resulting mixture was boiled for 4 hours. The mixture was treated with another 6 g. of potassium cyanide and boiled under reflux another 4 hours. After cooling, the re-

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(5) I. A. Pearl and D. L. Beyer, THIS JOURNAL, **74**, 4263 (1952).

action mixture was diluted with water. The aqueous solution was decanted from the resulting oil, and the oily residue was washed with water twice by decantation. The residue was boiled with ethanol in an attempt to isolate the desired XV, but cooling of the solution yielded only a resinous solid. This solid was redissolved by boiling, and the hot solution was poured into 1800 cc. of mixed Fehling solution at 50°. The resulting mixture was boiled under reflux for 2 hours and allowed to cool. The cooled mixture was extracted with ether, and the ether was dried and distilled to yield an orange-colored heavy oil. The oil was covered with methanol, warmed to effect solution, boiled with carbon and filtered. Upon cooling, the solution deposited light yellow crystals of XVI melting at 108–109°. Recrystallization from methanol raised the melting point to 110–111°. The ultraviolet absorption spectrum indicated one maximum: $\lambda_{max.}$ 292 mμ, ϵ 18800.

Anal. Calcd. for $C_{36}H_{34}O_6$: C, 76.85; H, 6.09. Found: C, 76.96; H, 6.13.

Debenzylation of 5,5'-Dipropenylvanillil Bis-benzyl Ether.—The crystals of XVI were covered with acetic anhydride and treated with a few drops of perchloric acid as described earlier.[6] After standing for 30 minutes at room temperature, the mixture was poured into excess water. The precipitate was filtered and recrystallized twice from ethanol to give crystals of XI melting at 179–180° and having an ultraviolet absorption spectrum with the maxima: $\lambda_{max.}$ 275 mμ, ϵ 15900; $\lambda_{max.}$ 322 mμ, ϵ 11700.

Anal. Calcd. for $C_{26}H_{26}O_8$: C, 66.94; H, 5.62. Found: C, 66.86; H, 5.69.

Acknowledgment.—The author wishes to thank Mr. Harold Willemsen for the analyses and spectra reported in this paper.

[6] I. A. Pearl, This Journal, **76**, 3635 (1954).

Appleton, Wisconsin

[Contribution from the Research Division, Canadian Breweries Limited]

Components of the Lead-precipitable Fraction of *Humulus lupulus*. Adhumulone.

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Adhumulone, a new component detected earlier in the lead-precipitable fraction of a hop extract, has now been isolated by countercurrent distribution followed by crystallization as the *o*-phenylenediamine complex. The empirical formula, $C_{21}H_{30}O_5$, shows adhumulone to be an isomer of humulone. Close structural similarity to humulone is indicated by other properties, including infrared spectra, which are reported. When boiled in mildly alkaline solution, adhumulone is transformed readily to isoadhumulone, comparable to but not identical with isohumulone. Hydrolysis of adhumulone in 1.5 *N* NaOH yields a new compound, *adhumulinic acid*.

The authors have shown previously[1,2] that the lead-precipitable fraction of a hop extract is a mixture containing significant amounts of two new components, cohumulone and adhumulone, in addition to humulone which formerly was believed to comprise most of this fraction. The first of these new substances to be detected, cohumulone, has been isolated earlier and some of its properties have been studied.[2,3] The investigation of the composition of the lead-precipitable fraction has been continued and the present report describes the isolation and properties of adhumulone.

The countercurrent distribution pattern, Fig. 1, for the lead-precipitable fraction (604 mg.) of California Seedless hops clearly shows the presence of the three principal components, cohumulone, humulone and adhumulone, with partition coefficients of 0.15, 0.29 and 0.48, respectively. This pattern was obtained after 350 transfers in a 100-tube apparatus using the single withdrawal procedure. The solvent system consisted of 2,2,4-trimethylpentane over a buffer composed of 74 volumes of *M* K_2HPO_4 adjusted to *p*H 7.25 with concentrated H_3PO_4, plus 26 volumes of reagent grade methanol.

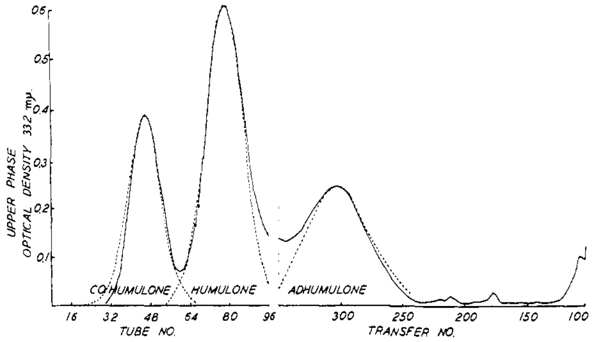

Fig. 1.—Distribution pattern for the lead-precipitable fraction of California Seedless hops, 1952. Solid line shows experimental pattern and dotted lines show theoretical curves.

Traces of minor components emerged from the train from transfer 125 to transfer 225. A mixture of substances having very high partition ratios, and amounting to approximately 5% of the total material distributed, was withdrawn in transfers 100 to 120. A mixture of substances having low partition ratios, also amounting to about 5% of the total material, did not move beyond the first ten tubes of the apparatus.

Distribution of the lead-precipitable fraction of extracts of other hop varieties yields similar patterns, the combined humulone, cohumulone and adhumulone usually comprising 85 to 90% of this fraction. The adhumulone content, expressed as percentage of the total of the three components, ranged from 10 to 15% among the samples examined.

The partition isotherms for these substances become non-linear at high concentration levels due to the low solubility of the substances in the aqueous phase. In consequence, when large loads of material (20–30 g.) are distributed, as in the isolation of substantial amounts of the components, such distributions depart considerably from the theoretical behavior shown in Fig. 1, and a much

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[1] F. L. Rigby and J. L. Bethune, This Journal, **74**, 6118 (1952).

[2] F. L. Rigby and J. L. Bethune, *Am. Soc. Brewing Chemists Proc.*, 119 (1953).

[3] G. A. Howard and A. R. Tatchell, *Chemistry & Industry*, 436 (1953).