*Anal.* Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25; neut. equiv., 244.3. Found: C, 78.17; H, 8.34; neut. equiv., 245.4.

The ultraviolet absorption spectra were determined between 220 and 300 mμ with a Beckman DU spectrophotometer. A concentration of 0.01% in absolute ethanol was employed in each case.

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## Reactions of Vanillin and Its Derived Compounds. XXVIII.[1] Coniferaldehyde and *p*-Coumaraldehyde

Irwin A. Pearl and Stephen F. Darling[2]

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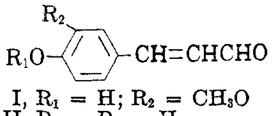
In connection with other studies in these laboratories on reactions of lignin, wood, and wood extractives, it was necessary to prepare substantial quantities of coniferyl aldehyde (I) and *p*-coumaraldehyde (II). These aldehydes had been prepared recently by Freudenberg and co-workers[3,4] by the stannous chloride reduction of the phenylimidochlorides of the corresponding acetylated acids, but the procedures involved did not lend themselves to quantity production. Attempts to adapt the Rosenmund procedure as used by Freudenberg and Hübner[5] for the preparation of the closely related sinapyl aldehyde resulted only in the recovery of the acid chlorides as their parent acids. The elegant method of Brown and McFarlin[6] for the production of aldehydes by the reduction of acid chlorides with lithium tri-*t*-butoxyaluminohydride was tried on acetylferulic and acetyl *p*-coumaric acid chlorides. These acid chlorides gave good yields of acetylconiferyl aldehyde (III) and acetyl *p*-coumaraldehyde (IV), respectively, and the acetylated aldehydes yielded the desired coniferyl aldehyde and *p*-coumaraldehyde upon hydrolysis with sodium methylate in chloroform solution.



I, $R_1 = H$; $R_2 = CH_3O$
II, $R_1 = R_2 = H$
III, $R_1 = CH_3CO$; $R_2 = CH_3O$
IV, $R_1 = CH_3CO$; $R_2 = H$

EXPERIMENTAL

All melting points are uncorrected, and ultraviolet spectral data are for solution in 95% ethanol (concentration, 0.02 g. per liter).

*Lithium tri-t-butoxyaluminohydride.* The reagent was prepared by treating a filtered solution of lithium aluminum hydride in absolute ether with dry *t*-butyl alcohol with stirring. The white precipitate was filtered, washed with anhydrous ether, and dried at 60°.

*Acetylconiferylaldehyde* (III). A solution of 12.2 g. (0.05 mole) of acetylferuoyl chloride[3] in 75 ml. of dry tetrahydrofuran was placed in a 250-ml. 3-neck flask fitted with a dropping funnel, thermometer, and mercury-sealed stirrer, and immersed in a Dry Ice–acetone bath. The solution was cooled to −65° and treated dropwise with stirring with a solution of 12.7 g. (0.05 mole) of lithium tri-*t*-butoxyaluminohydride in 50 ml. of dry tetrahydrofuran while maintaining the temperature at −65°. After addition was complete the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature with stirring. With rise in temperature, the turbid mixture became clear. When the temperature reached 20° the mixture was poured onto a mixture of crushed ice and water. The precipitate was filtered, and the filtrate deposited colorless platelets upon standing. These were collected, and the filtrate was concentrated and cooled to give more platelets. The total yield of platelets melting at 95–96° was 1.2 g. The original aluminum hydroxide precipitate was extracted with boiling ethanol, and the ethanol was concentrated in a rotating evaporator to yield 5.0 g. of product melting at 81–97°. Both of these products, when adsorbed on aluminum oxide and eluted with ether, yielded pure pale yellow crystals of III melting at 97–98° and having the following maxima in its ultraviolet absorption spectrum: $\lambda_{max}$ 240 mμ, $\epsilon$ 11800; $\lambda_{max}$ 290 mμ, $\epsilon$ 19440.

*Anal.* Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.67; H, 5.49.

Freudenberg and Dillenburg[3] reported a melting point of 102–103° for III prepared by acetylation of isolated I, but repetition of their work in this laboratory confirmed the 97–98° melting point.

This experiment was repeated with diglyme as the solvent with essentially the same results.

*Coniferaldehyde* (I). A solution of 2 g. of III in 50 ml. of chloroform was treated with cooling with a solution of 0.5 g. of sodium in 10 ml. of anhydrous methanol. The mixture was allowed to stand at 20° for 30 min., and then treated with 50 ml. of water. The mixture was shaken, and the aqueous layer was separated and acidified with dilute sulfuric acid. The acidified mixture was extracted with chloroform, and the chloroform was dried and concentrated to dryness. The residual sirup was covered with a little benzene and scratched to induce crystallization. The crude crystals melted at 70–72°, and the material obtained upon recrystallization from benzene melted at 80–81° and did not depress the melting point of authentic coniferaldehyde.[3] The yield was 75%.

*Acetyl p-coumaraldehyde* (IV). Similar reduction of 11.2 g. of acetyl *p*-coumaroyl chloride (m.p. 119–121° from benzene–petroleum ether) in diglyme or tetrahydrofuran as a solvent yielded 7 g. of crude IV melting at 70–75° which, upon recrystallization from ether-petroleum ether, yielded colorless crystals of IV melting at 77–78° and having the following maxima in its ultraviolet absorption spectrum: $\lambda_{max}$ 223 mμ, $\epsilon$ 14800; $\lambda_{max}$ 293 mμ, $\epsilon$ 24750.

*Anal.* Calcd. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.32; H, 5.17.

The *semicarbazone*, after crystallization from ethanol, melted at 213–215°.

*Anal.* Calcd. for $C_{12}H_{13}O_3N_3$: C, 58.29; H, 5.30. Found: C, 58.46; H, 5.26.

*p-Coumaraldehyde* (II). Reduction of IV with a solution of sodium methylate in methanol-chloroform as described

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(1) For paper XXVII of this series, see *J. Org. Chem.*, **22**, 1229 (1957).

(2) Lawrence College, Appleton, Wis.

(3) K. Freudenberg and R. Dillenburg, *Chem. Ber.*, **84**, 67 (1951).

(4) K. Freudenberg and G. Gehrke, *Chem. Ber.*, **84**, 443 (1951).

(5) K. Freudenberg and H. H. Hübner, *Chem. Ber.*, **85**, 1181 (1952).

(6) H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **78**, 252 (1956).

above gave an almost quantitative yield of II which was recrystallized from benzene to yield slightly yellow crystals melting at 138–140°, which was the melting point recorded for II prepared by reduction of acetyl *p*-coumaric acid phenylimidochloride with stannous chloride.[4]

Acknowledgment. The authors wish to thank the Analytical Department of The Institute of Paper Chemistry for the analyses and spectra reported in this paper.

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# Urethanes of Tropine and Phenylmethylpyrazolone

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Some years ago, when these laboratories were engaged in the synthesis of cholinergic drugs, it became desirable to prepare the dimethylurethanes of tropine and of phenylmethylpyrazolone and to study pharmacologically these substances and some of their quaternary salts.

## EXPERIMENTAL

*Tropine*, m.p. 63–64°, could be obtained from atropine in 85–95% yield by refluxing 20–25 min. with alcoholic potassium hydroxide, followed by rapid ethereal extraction of the cooled diluted solution (Tropic acid, m.p. 105–106°, could be isolated from the acidified alkaline solution).

*Dimethylcarbamoyltropine.* Equal weights of tropine and dimethylcarbamoyl chloride were rapidly heated to 150–160°. The color of the mixture changed to reddish brown and on cooling the mixture solidified. The pulverized solid was extracted with benzene and then dissolved in water. The aqueous solution was made basic with sodium carbonate, extracted with chloroform, and the solvent stripped from the extract to leave the crude product. This could be purified *via* the picrate (chromatographed on alumina) but this procedure offered little advantage over direct distillation. The pure product distilled at 105–120° (1 mm.) without decomposition and was obtained in 38 to 46% yield. It was a colorless liquid, soluble in water, benzene, alcohol, and ether.

*Anal.* Calcd. for $C_{11}H_{20}N_2O_2$: C, 62.26; H, 9.43; N, 13.20. Found: C, 62.52; H, 9.62; N, 12.89.

The *picrate* was prepared in the usual manner and melted at 210–212° after recrystallization from alcohol.

*Anal.* Calcd. for $C_{11}H_{20}N_2O_2\cdot C_6H_3N_3O_7$: C, 46.26; H, 5.25; N, 15.80. Found: C, 46.09; H, 4.88; N, 16.33.

The methiodide was prepared by interaction of the urethane and methyl iodide in methanol. It melted at 250–252° after recrystallization from methanol and ether.

*Anal.* Calcd. for $C_{11}H_{20}N_2O_2\cdot CH_3I$: C, 40.67; H, 6.49; N, 7.90. Found: C, 40.86; H, 6.77; N, 7.74.

The *methobromide* was prepared by the addition of a dry benzene solution of the urethane to a solution of an excess of methyl bromide in benzene. It melted at 280–283° after recrystallization from methanol and ether.

*Anal.* Calcd. for $C_{11}H_{20}N_2O_2\cdot CH_3Br$: C, 46.89; H, 7.55; N, 9.11. Found: C, 46.61; H, 7.58; N, 9.13.

The *benzochloride* was so hygroscopic that it could not be obtained pure. The *benzobromide* was prepared by the interaction of the urethane and benzyl bromide in boiling benzene. It melted at 250–252° after recrystallization from ethanol and ether.

*Anal.* Calcd. for $C_{11}H_{20}N_2O_2\cdot C_7H_7Br$: C, 56.39; H, 7.10; N, 7.31. Found: C, 55.61; H, 7.28; N, 7.01.

*1-Phenyl-3-methyl-5-dimethylcarbamoyloxypyrazole.* Equal weights of the dry potassium salt of 1-phenyl-3-methyl-5-pyrazolone and dimethylcarbamoyl chloride were heated on the steam bath for 15 min. and the mixture was then leached with chloroform. The chloroform solution was washed with aqueous sodium carbonate, dried, and distilled to give 45–50% yields of product, b.p. 167–172° (2–3 mm.).

*Anal.* Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.67; H, 6.12. Found: C, 63.98; H, 6.40.

This material did not give a picrate, methiodide, or benzochloride (no picrate or quaternary salts of phenylmethylpyrazolone are reported in the literature).

The methiodide and benzobromide of dimethylcarbamoyltropine showed no cholinergic effect on isolated guinea pig intestine at a concentration of 100 γ/cc. (determined by Dr. R. J. Schachter).

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# Reaction of NBS with Allylic Alcohols

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In connection with previous studies[2] on selective oxidations of secondary alcohols with *N*-bromosuccinimide, the oxidation of the steroid allylic alcohols was investigated. $\Delta^4$-Cholestene-3β,6β-diol was oxidized mainly to 3,6-cholestanedione (42% yield), presumably through the intermediate formation of $\Delta^4$-cholestene-6β-ol-3-one, which was indeed isolated also but in low yield (17%). The results contrast with those obtained with the corresponding saturated 3β,6β-diol,[2] where only the 6β-hydroxyl group is affected, but are understandable in terms of a half-chair conformation for Ring A in the unsaturated diol.[3]

In the reaction of *N*-bromosuccinimide with 7β-hydroxycholesterol, neither of the hydroxyl groups is oxidized; instead a bromohydrin is obtained (57% yield). This is converted into an oxide when treated with base. This oxide and the isomeric oxide were both obtained by oxidation of $\Delta^5$-cholestene-3β,7β-diol with perphthalic acid. The

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[1] This investigation was carried out during 1954 in the Department of Chemistry, Harvard University, under a grant from the Camille and Henry Dreyfus Foundation. Present address: Productos Esteroides S.A., México City.

[2] L. F. Fieser, H. Heymann, and S. Rajagopalan, *J. Am. Chem. Soc.*, **72**, 2306 (1950); L. F. Fieser and S. Rajagopalan, *J. Am. Chem. Soc.*, **71**, 3935 (1949); **71**, 3938 (1950); **72**, 5530 (1950).

[3] E. J. Corey and R. A. Sneen, *J. Am. Chem. Soc.*, **77**, 2505 (1955).