structure of IV. Such a scheme seemed less likely to us. Our expectation that 2-vinylpyridine would be reduced too rapidly to 2-ethylpyridine and subsequently to 2-ethylpiperidine to allow III to form was confirmed when it was hydrogenated in the presence of II at 150° and 130 atm. with Raney nickel. 2-Ethylpiperidine was obtained in over 80% yield. Additional material boiling slightly higher than 2-ethylpiperidine (possibly contaminated with 2-ethylpyridine) raised the consumption of 2-vinylpyridine to 97%. Seventy per cent of II was recovered.

Experimental[4]

1-[2-(2-Piperidyl)ethyl]-2-(2-hydroxyethyl)piperidine (IV).—A solution of 87.0 g. (0.7 mole) of 2-(2-hydroxyethyl)pyridine in 150 ml. of absolute ethyl alcohol was hydrogenated at 150° and 130 atm. in the presence of 12.0 g. of commercial Raney nickel. Uptake of hydrogen was usually complete in 8–15 hr. After removal of the catalyst and distillation of the solvent, the residue was fractionated. After collection of the fraction boiling at 85–87° (0.3 mm.), which gave an unsatisfactory analysis for 2-(2-hydroxyethyl)piperidine,[5] the remaining portion was collected at 142–156° (0.3 mm.): $n^{25}D$ 1.4977, 8% yield. The material solidified and was recrystallized from hexane: m.p. 92–96°, $\lambda_{max}^{CCl_4}$ 1.42 (OH) and 1.55 μ (NH), $\lambda_{max}^{CHCl_3}$ no pyridine bands.

Anal. Calcd. for $C_{14}H_{28}N_2O$: C, 69.95; H, 11.74; N, 11.66. Found: C, 70.29; H, 11.78; N, 11.95.

Proof of Structure of IV. Preparation of III.—Following a recently described procedure,[6] a solution of 103.2 g. (0.8 mole) of 2-(2-hydroxyethyl)piperidine, 42.0 g. (0.4 mole) of freshly distilled 2-vinylpyridine, 150 ml. of methyl alcohol, and 12.0 g. (0.2 mole) of glacial acetic acid was heated in a 1-l. stainless steel rocker-type bomb for 24 hr. at 65–70°. The reaction mixture was concentrated and the residue was dissolved in water and treated with excess 50% sodium hydroxide solution. The oily layer which separated was dissolved in ether and the remainder of the solution was extracted several more times. After drying the extract over anhydrous magnesium sulfate, removal of the drying agent, and distillation of solvent, the residue was fractionated. After recovery of excess 2-(2-hydroxyethyl)-piperidine, 1-[2-(2-pyridyl)ethyl]-2-(2-hydroxyethyl)piperidine (III) was obtained in 34% yield: b.p. 175–178° (2.4–2.5 mm.); $n^{25}D$ 1.5307; λ_{max}^{film} 3.05 (broad, OH), 6.27, 6.36, and 6.78 μ (pyridine).

Anal. Calcd. for $C_{14}H_{22}N_2O$: C, 71.75; H, 9.47; N, 11.95. Found: C, 71.47; H, 9.82; N, 11.90.

Hydrogenation of III to IV.—A solution of 23.4 g. (0.1 mole) of III in 100 ml. of ethyl alcohol was hydrogenated at 60° and 3 atm. in the presence of 10 g. of 5% rhodium on alumina. Uptake of hydrogen was complete before reaction temperature was reached (0.5 hr.). The solution was filtered from the catalyst which was washed with additional alcohol. After removal of the solvent under reduced pressure, the residue solidified on treatment with hexane and seeding with a crystal of known product. The material was treated with cold hexane and filtered. A yield of almost 92% of IV was obtained melting at 95–97°, not depressed when mixed with known material. It was analyzed without further purification.

Anal. Calcd. for $C_{14}H_{28}N_2O$: C, 69.95; H, 11.74; N, 11.66. Found: C, 69.81; H, 11.61; N, 11.61.

Reduction of I in the Presence of II.—A mixture of 61.5 g. (0.5 mole) of 2-(2-hydroxyethyl)pyridine and 64.5 g. (0.5 mole) of 2-(2-hydroxyethyl)piperidine was hydrogenated at 160° and 120 atm. in the presence of 13–15 g. of Raney nickel. At the end of 5 hr. 3 equiv. of hydrogen were absorbed. When the reaction mixture was cool, it was filtered and the catalyst was rinsed with ethyl alcohol. The solvent was concentrated under reduced pressure and the residue was then fractionated. After collection of 53 g. of II, a higher boiling fraction, b.p. 197° (4.3 mm.), was collected, yield 6%. It solidified and melted at 91°. Its infrared spectrum was identical with IV.

The remaining material which solidified in the distillation flask was dissolved in 200 ml. of anhydrous ether and treated with alcoholic hydrogen chloride until the mixture was acidic. On standing, a sticky mass formed. Decanting the solvent and treating the material with dry acetone made it filterable. It was then recrystallized by dissolving in hot absolute alcohol and adding the solution to several volumes of anhydrous ether. It was identified as the dihydrochloride salt of IV: m.p. 150° with preliminary softening; 2% yield.

Anal. Calcd. for $C_{14}H_{30}Cl_2N_2O$: C, 53.66; H, 9.65; Cl, 22.63; N, 8.95. Found: C, 53.59; H, 10.02; Cl, 22.65; N, 9.10.

Hydrogenation of a Mixture of 2-Vinylpyridine and II.—A solution of 0.4 mole of II and 0.4 mole of freshly distilled 2-vinylpyridine in 125 ml. of ethyl alcohol was treated with hydrogen at 150° and 120-atm. pressure in the presence of 20 g. of Raney nickel. Uptake of hydrogen started at 100°; at 160°, uptake was about 3.5 equiv., indicative of conversion of 2-vinylpyridine to 2-ethylpiperidine. Reaction was continued for several hours. After cooling and removal of the catalyst, the solution was distilled through a packed column. The alcohol which was collected was strongly basic. It was treated with alcoholic hydrogen chloride until acidic and concentrated to dryness. The dried salt (22.0 g.) melted at 182°. The melting point was not depressed when mixed with an authentic sample of 2-ethylpiperidine hydrochloride. More 2-ethylpiperidine as base was collected at 135–140° (atmospheric pressure): $n^{25}D$ 1.4469. The total yield of pure material was 86%. Two slightly higher boiling fractions, b.p. 70° (50 mm.), $n^{25}D$ 1.4474, and b.p. 79° (36 mm.), $n^{25}D$ 1.4484, weighing a total of 8.0 g. were also obtained. From the boiling points, *ca.* 150° and 160° at atmospheric pressure, and the refractive indices they appeared to be 2-ethylpiperidine contaminated with some 2-ethylpyridine. This raised the yield of 2-ethylpiperidine to 97%. About 35.0 g. of II was recovered (70%).

Effect of Hydrogenation Conditions on II.—A solution of 51.6 g. (0.4 mole) of II in 250 ml. of ethyl alcohol was heated and rocked in a 1-l. stainless steel bomb for 3 hr. at 150° and 120 atm. in the presence of 10–15 g. of Raney nickel. After cooling and removal of catalyst, the solution was distilled at atmospheric pressure. The alcohol which was collected was basic. It was neutralized with alcoholic hydrogen chloride and concentrated to dryness. A salt, 3 g., was obtained; m.p. 210°. The next fraction (8.0 g.) distilled at 115–120° (described for 2-methylpiperidine, 119°). It was converted to the hydrochloride salt, m.p. 210°, not depressed on mixing with a known sample. The total yield of 2-methylpiperidine was about 25%. Close to 70% of II was recovered: b.p. 128° (20 mm.), $n^{25}D$ 1.4842.

(4) Melting points were taken on Fisher-Johns apparatus and are not corrected. Microanalyses were carried out by Mr. O. F. Kolsto and his group, infrared and near-infrared spectra by A. Kammer and W. Washburn.

(5) From the consistently high carbon values it appeared that the fraction was likely a mixture of II and the 1-ethyl derivative of II resulting from reduction conditions in the presence of alcohol: M. Freifelder, *Advan. Catalysis*, **14**, 206 (1963).

(6) G. M. Singerman and R. Levine, *J. Heterocyclic Chem.*, **1**, 151 (1964), method A.

The Claisen Rearrangement of Resorcinol Monoallyl Ether

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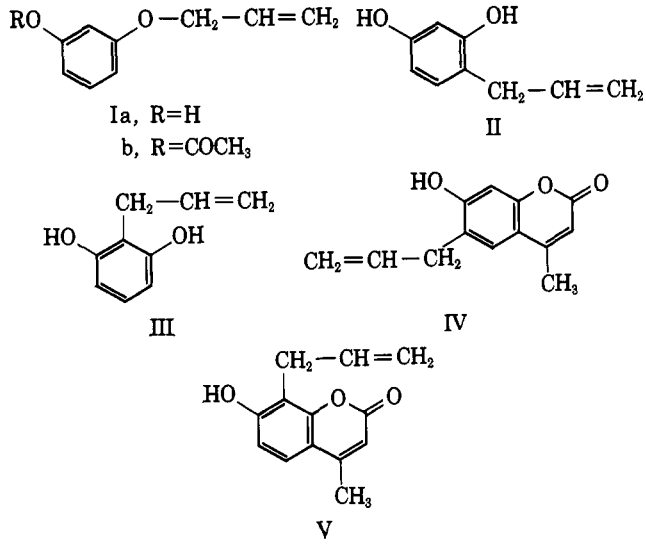
It has been reported[1] that resorcinol monoallyl ether (Ia) rearranges to 4-allylresorcinol (II) at temperatures between 170 and 280°. Nesmejanow and Sarewitsch[1b] obtained a crystalline sample of II, m.p. 67°, although Hurd, *et al.*,[1a,c] were unable to isolate any crystalline products from the rearrangement. None of the previous workers reported 2-allylresorcinol (III) as a product of the rearrangement.

(1) (a) C. D. Hurd, H. Greengard, and F. D. Pilgrim, *J. Am. Chem. Soc.*, **52**, 1700 (1930); (b) A. N. Nesmejanow and T. S. Sarewitsch, *Ber.*, **68**, 1476 (1935); (c) C. D. Hurd and M. P. Puterbaugh, *J. Org. Chem.*, **2**, 381 (1937).

This reaction has been reinvestigated with the aid of a spinning-band fractionating column and vapor phase chromatography. Pure resorcinol monoallyl ether (Ia) was obtained by alkaline hydrolysis of 3-allyloxyphenyl acetate[2] (Ib), which is readily obtained by allylation of resorcinyl monoacetate. To avoid complications due to the exothermic nature of the reaction,[1a] the Claisen rearrangement of Ia was carried out in refluxing diethylaniline, and a red oil was obtained in 94% yield. Distillation through a spinning-band column facilitated the isolation of small crystalline samples of 4-allylresorcinol (II), m.p. 68–69°, and 2-allylresorcinol (III), m.p. 48–52°. The identity of both compounds was confirmed by condensation of each with ethyl acetoacetate to obtain 6-allyl-4-methylumbelliferone (IV) and 8-allyl-4-methylumbelliferone (V). The latter compound was shown to be identical (mixture melting point and infrared spectra) with an authentic sample.[2]



In order to estimate its percentage composition, a small portion of the crude Claisen rearrangement product was subjected to simple distillation, to remove traces of colored impurities, and analyzed by vapor phase chromatography. Estimation of the areas under the curves showed that the mixture was 57% 2-allylresorcinol (III) and 43% 4-allylresorcinol (II).

In contrast with the results of earlier workers[1], who emphasize 4-allylresorcinol as the product of Claisen rearrangement of resorcinol monoal yl ether, this study indicates that the 2-allyl isomer is also formed, and in slightly larger amounts. It should be mentioned that the 4-allyl isomer crystallizes more readily and hence is more easily isolated.

Experimental[3]

Resorcinol Monoallyl Ether (Ia).—Crude, undistilled 3-allyloxyphenyl acetate[2] (20 g., 0.104 mole) was refluxed in a stirred, 10% aqueous sodium hydroxide solution under a nitrogen atmosphere for 2 hr. The cooled solution was shaken with ether (*ca.* 150 ml.) and then poured into a stirred mixture of ice and concentrated hydrochloric acid (100 ml.). A brown oil separated and was isolated with ether. Vacuum distillation gave 9.24 g. (59.2%) of a yellow oil, b.p. 102° at 0.7 mm. Evaporation of the first ether extract led to the recovery of 4.0 g. of unreacted starting material.

Claisen Rearrangement.—A mixture of resorcinol monoallyl ether (62.89 g.) and diethylaniline (125 ml.) was refluxed for 1 hr. An ether solution of the reaction mixture was extracted with 5% aqueous sodium hydroxide and the acidified (concentrated hydrochloric acid) alkaline layer was extracted with ether. The ether layer was washed with 5% aqueous sodium bicarbonate (to remove traces of hydrochloric acid, which cause extensive decomposition during distillation), dried ($MgSO_4$), and concentrated to a red oil (59.09 g., 94%). A portion of this oil (16.77 g.) was carefully distilled through an 18-in., stainless steel, spinning-band column.[4] After a negligible forerun, a fraction (5.108 g., b.p. 88–90.5° at 0.15 mm.) was obtained and it crystallized after standing for several days. Repeated crystallization of a portion of this fraction from a mixture of benzene and petroleum ether (b.p. 30–60°) gave 2-allylresorcinol, m.p. 48–52° (lit.[1b] m.p. 52°). A later fraction (5.135 g., b.p. 99–100° at 0.15 mm.) also crystallized, and a portion of it was recrystallized twice from a mixture of benzene and petroleum ether (b.p. 30–60°) to give 4-allylresorcinol, m.p. 68–69° (lit.[1b] m.p. 67°).

8-Allyl-4-methylumbelliferone (IV).—Dry hydrogen chloride gas was passed through a solution of 2-allylresorcinol (50 mg.) and ethyl acetoacetate (0.04 ml.) in glacial acetic acid (*ca.* 3 ml.) for 45 min. After standing in a closed container for 14 hr., the reaction mixture was poured into water (*ca.* 30 ml.) and the precipitate was recrystallized once from 95% ethanol and twice from benzene to give colorless prisms, m.p. 196–197°. A mixture of this compound and a sample of 8-allyl-4-methylumbelliferone (m.p. 200–201°)[2] had m.p. 197–198°. The infrared spectra of the two samples were identical.

6-Allyl-4-methylumbelliferone (V).—Dry hydrogen chloride gas was passed through a solution of 4-allylresorcinol (0.20 g.) and ethyl acetoacetate (0.17 ml.) in glacial acetic acid (*ca.* 8 ml.) for 45 min. After standing in a closed container for 12 hr., the reaction mixture was poured into water (*ca.* 80 ml.) and the cream-colored precipitate was recrystallized from a mixture of ethanol and water to give colorless needles (0.201 g., 69%), m.p. 174–175° (lit.[2] m.p. 175–176°).

Vapor Phase Chromatography.—The crude reaction product from the Claisen rearrangement of resorcinol monoallyl ether was purified by simple distillation at 125° at 0.4 mm. to give a colorless oil (95% recovery). A 20% solution in ethanol (2 μl.) was introduced at an injection port temperature of 245° on a 2 ft. × 0.125 in. stainless steel column of SE-30 silicone rubber suspended on firebrick as supplied with an F and M (Model 500) gas chromatograph. The column temperature was maintained at 175° and helium flowed continuously through the column at a rate of 80 ml./min. Under these conditions, pure 2-allylresorcinol was retained on the column for 2.7 min. and 4-allylresorcinol for 3.5 min. The areas under the curves were estimated by multiplying the height of a peak by its half-width.

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(2) K. D. Kaufman, *J. Org. Chem.*, **26**, 117 (1961).

(3) All melting points were determined on a Fisher-Johns melting point apparatus and are corrected.

(4) Nester and Faust, Box 565, Newark, Del.

Preparation and Resolution of Cyclopentaneglycine[1]

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The synthesis and microbiological properties of the isoleucine analog DL-cyclopentaneglycine have

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