The Synthesis of Linalool

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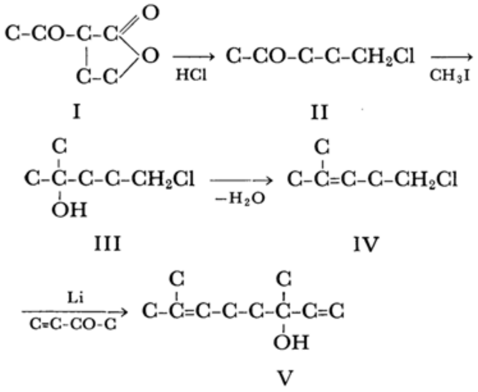
Linalool is widely used in perfumery. Various methods have been used successfully for the synthesis of linalool. The authors will now describe a new method of preparing linalool from α-acetyl-γ-butyrolactone (I), which is an intermediate of vitamin B_1[1]. This new method is shown in the following scheme:



5-Chloro-2-pentanone (II) was prepared by the action of aqueous hydrochloric acid[2] on I in a good yield. The ketone (II) with methylmagnesium iodide gave the alcohol 1-chloro-4-methyl-4-hydroxy-pentane (III) in a 60% yield. The alcohol (III) was then dehydrated easily by potassium bisulfate to 1-chloro-4-methyl-3-pentene (IV). The alkenyl lithium from the chloride (IV) reacted with methylvinyl ketone to give linalool (V). The identity of V was confirmed by comparing its infrared absorption spectrum and its gas liquid chromatography with those of authentic linalool.

Similarly, dihydrolinalool was prepared from the alkenyl lithium of the chloride (IV) and ethyl methyl ketone.

Experimental

α-Acetyl-γ-butyrolactone (I). — It was obtained from the Sankyo Co., Ltd., and from the Takasago Perfumery Co., Ltd.

5-Chloro-2-pentanone (II).—A mixture of 45 ml. of concentrated hydrochloric acid, 53 ml. of water, and 38.4 g. (0.3 mol.) of I was placed in a 200 cc. distilling flask fitted with a condenser and a receiver immersed in an ice-water bath. The reaction mixture was heated for 10 min., and then distilled as rapidly as possible. After 90 ml. of distillate had been collected, 50 ml. of water was added to the distilling flask and another 30 ml. of distillate was collected. The yellow organic layer was extracted with ether. The ether extracts were dried over calcium chloride. Fractional distillation gave a crude II (28 g., yield 78%). It was redistilled for characterization, b. p. 70—72°C/12 mmHg; n_D^{25} 1.4371 (reported[2] 70—72°C/12 mmHg, n_D^{25} 1.4371).

1-Chloro-4-methyl-4-hydroxypentane (III).—Methylmagnesium iodide, obtained from magnesium (4 g.) and methyl iodide (22 g.) in ether (200 ml.), was cooled to 0°C and stirred during the addition (10 min.) of II (20 g.) in ether (100 ml.). After a further 60 min., acetic acid (25 ml.) in ether (50 ml.) was added. The mixture was then stirred with water (200 ml.), and the aqueous layer was extracted with ether. The ether extracts were washed with aqueous sodium hydrogen carbonate, dried over anhydrous sodium sulfate, and distilled to give 1-chloro-4-methyl-4-hydroxypentane (III) (8 g.), b. p. 80—83°C/16 mmHg; d_4^{20} 1.1091; n_D^{20} 1.4522; IR: ν_{max} 3380 cm^{-1} (OH), ν_{max} 1120 cm^{-1} (a tertiary OH), the gas chromatogram showed a single peak.

1-Chloro-4-methyl-3-pentene (IV). — The above chloride (III) (8 g.) was heated at 160°C with fine-powdered potassium bisulfate (2 g.). After an hour 10 ml. of water was added, and the mixture was extracted with ether. The ether extracts were dried over anhydrous sodium sulfate. Fractional distillation gave 1-chloro-4-methyl-3-pentene (IV) (4.5 g.), b. p. 125—130°C; d_4^{20} 0.9721; n_D^{20} 1.4414; IR: ν_{max} 890 cm^{-1} ($-\overset{|}{C}{=}CH$); gas chromatography showed a single peak.

Linalool (IV).—Lithium (0.47 g.; thin strips freshly cut) and ether (50 cc.) under nitrogen were stirred during the slow addition of 1-chloro-4-methyl-3-pentene (IV) (4 g.) in ether (60 cc.). When reaction began, a cooling bath (−20°C) was applied. Stirring was then continued at −15°C until nearly all the lithium had reacted (2 hr.). To the solution at −70°C, methyl vinyl ketone (2.3 g.) in ether (10 cc.) was added (5 min.). Twelve hours later a 50% alcoholic solution (10 cc.) in ether was added, and the mixture was treated as usual. Fractional distillation gave 3 g. of linalool (V), b. p. 78—80°C/6 mmHg; d_4^{15} 0.8702; n_D^{20} 1.4681; IR: 3400 cm^{-1} (OH), 1120 cm^{-1} (a tertiary OH), 890 cm^{-1} ($-\overset{|}{C}{=}CH-$), 910 and 990 cm^{-1} ($-CH{=}CH_2$).

Its nature was confirmed by comparing its infrared absorption spectrum and gas chromatography with those of an authentic sample. (Found: C, 77.80; H, 11.73%).

Dihydrolinalool (VI).—Much as has been described above, dihydrolinalool was prepared from 1-chloro-4-methyl-3-pentene (IV) and ethyl methyl ketone. The dihydrolinalool so prepared had the following

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[1] E. R. Buchman, *J. Am. Chem. Soc.*, **58**, 1803 (1936).

[2] G. W. Cannon, R. C. Ellis and J. R. Leal, "Organic Syntheses," Vol. 31, 74 (1951).

properties: b. p. 92.5—93°C/13 mmHg; n_D^{17} 1.4568; d_4^{17} 0.8573 (reported[3] b. p. 94—94.5°C/14 mmHg; n_D^{15} 1.4569; d_4^{15} 0.8695; d_4^{17} 0.8572); IR: 3400 cm^{-1} (OH), 1150 cm^{-1} (OH), 890 cm^{-1} ($-\overset{|}{C}=CH-$). The infrared absorption spectrum and gas chromatography of VI agreed with those of an authentic sample (VI). (Found: C, 76.83; H, 12.81%)

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[3] H. Wienhaus and W. Treibs, *Ber.*, **56**, 1651 (1923); Beilstein **I**, 452.