A STUDY OF THE SUBSTANCES COMPOSING ESSENTIAL OILS

XXVIII. The Synthesis of α-Fenchylpelargonic Acid

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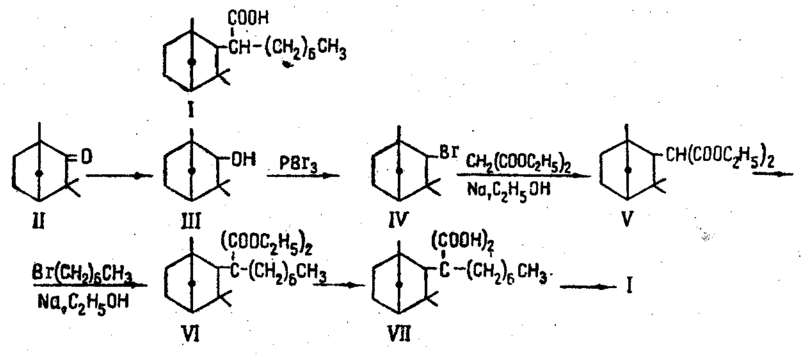
In recent years the synthesis of physiologically active substances based on terpenoids forming components of essential oils has been carried out [1, 2]. Thus, the cedrenecarboxylic acid synthesized from cedrol has shown a considerable activity as a growth stimulator for nightshade and tobacco.

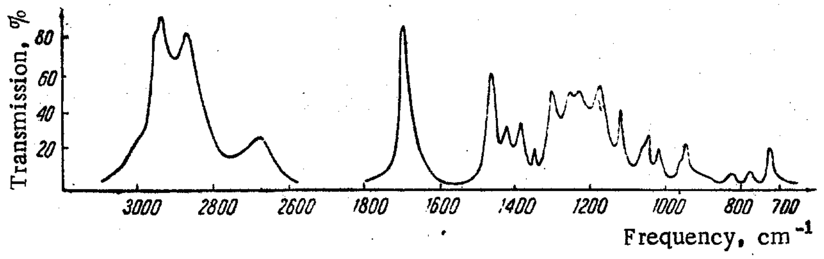
We have synthesized acids starting from terpene compounds containing 5- and 6-membered rings with prolongation of the side chain in order to determine their growth activity.

In the present paper we give the results of the synthesis of α-fenchylpelargonic acid (I). To synthesize this acid, we started with d-fenchone (II), which was subjected to various transformations.



The purity of the intermediate reaction products was checked by thin-layer chromatography in alumina and gas-liquid chromatography (UKh-1 instrument) with a copper column (250 × 0.6 cm).

Polyethylene glycol-2000 deposited on the solid support INZ-600 with a particle size of 0.35–0.45 mm was used as the stationary liquid phase. The molecular weight of the acid (I) was found from its neutralization equivalent, its elemental analysis was determined, and its IR spectrum was taken on a UR-10 instrument (figure).



IR spectrum of α-fenchylpelargonic acid (NaCl and LiF prisms).

Experimental

Fenchol. A 0.75-*l* round-bottomed three-necked flask fitted with a stirrer and reflux condenser was charged with 7 g of a suspension of lithium aluminum hydride in 300 ml of absolute ether. To the suspension was added 50 g of d-fenchone (II) (n_D^{20} 1.4625) dissolved in absolute ether [3]. The reaction began rapidly. After the addition of all of the fenchone, the mixture was heated on a boiling water bath for 2 hr. Then the excess of lithium aluminum hydride was decomposed first with moist ether and then with 10–15% sulfuric acid. The ethereal layer was poured off and the residue was washed several times with ether. The combined ethereal solutions were dried over anhydrous magnesium sulfate. After the ether had been evaporated, the residue was distilled under vacuum. This gave 32.6 g of fenchol (III). Yield 65% of theoretical, mp 44°–45° C (from alcohol).

Fenchyl bromide. With constant stirring, 15 ml of phosphorus tribromide was added in drops to 25 g of fenchol (III) dissolved in petroleum ether. The reaction mixture was cooled in such a way that the temperature did not exceed − 5° C. After the addition of all of the phosphorus tribromide, the reaction mixture was left to stand at room temperature for 24 hr. Then the solution was washed successively with water, sodium carbonate solution, and water again, and was dried with anhydrous calcium chloride. The petroleum ether was distilled off and the residue was distilled under vacuum. This gave 13.2 g of fenchyl bromide (IV). Yield 36% of theoretical, bp 65°–70° C/2 mm, n_D^{20} 1.5000.

Found, %: Br 35.9. Calculated for $C_{10}H_{16}Br$, %: Br 36.8.

Fenchylmalonic ester. Twenty grams of malonic ester was added to a solution of 2.8 g of metallic sodium in 50 ml of absolute alcohol. Slowly, in drops, 21 g of fenchyl bromide was added to this mixture and it was heated on a boiling water bath for 4–5 hr [4].

The solvent was distilled off and the solid residue obtained was dissolved in water. The diethyl ester (V) was extracted with ether. The ether was driven off and the residue was distilled under vacuum. This gave 18.1 g of fenchylmalonic ester (V). Yield 42% of theoretical, bp 79°–80° C/5 mm, n_D^{20} 1.4440.

Condensation of fenchylmalonic ester with heptyl bromide. One gram of metallic sodium was dissolved in 50 ml of ethanol and 12.1 g of fenchylmalonic ester was added and then, in drops, with stirring, 7.35 g of heptyl bromide. The mixture was heated on a boiling water bath under reflux for 6 hr. The alcohol was distilled off and the solid residue was dissolved in water, after which the reaction product was extracted with ether. After drying over anhydrous magnesium sulfate, the ether was evaporated off and the residue was distilled under vacuum. This gave 4.5 g of the ester of the dibasic acid (VI). Yield 27% of theoretical, bp 160°–165° C/2 mm, n_D^{20} 1.4465.

α-Fenchylpelargonic acid. In the boiling water bath, 4.5 g of the ester of the dibasic acid was saponified with a fivefold amount of a saturated alcoholic solution of caustic potash for 10 hr. The alcohol was distilled off and the residue was dissolved in the minimum amount of water and neutralized with 10% sulfuric acid.

The dibasic acid (VII) which separated out was extracted with ether and the ethereal solution was dried over anhydrous magnesium sulfate. The dibasic acid was not purified but was decarboxylated directly at 170°–180° C for 6–8 hr. The acid formed was vacuum-distilled. This gave 1.5 g of α-fenchylpelargonic acid (I). Yield 45.4% of theoretical, bp 160°–165° C/2 mm, n_D^{20} 1.4430.

Found, %: C 77.2, 77.4; H 11.35, 11.11; mol. wt. 299.1. Calculated for $C_{19}H_{32}O_2$, %: C 77.8; H 11.26; mol. wt. 293.0.

Summary

α-Fenchylpelargonic acid, a potential growth substance, has been synthesized.

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