Natural Furan Derivatives. Part I. The Synthesis of Perillaketone

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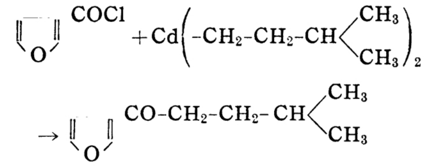
Perillaketone was isolated from the leaves of the Manchurian *Perilla frutescens Brit.* and was given the structural formula (I) by Goto[1]. Sebe also isolated perillaketone from the Formosan Perilla frutescens form viridis Kudo and independently gave the same formula (I) to it[2]. For the purpose of the confirmation of its structure, the present synthesis of β-furyl isoamyl ketone has been furnished.

The reaction of the acid chloride of 3-furcic acid with diisoamyl cadmium gave the desired β-furyl isoamyl ketone, which was purified with the Girard reagent P. The pure ketone has the similar physical constants to natural perillaketone, as are shown in Table I, and it gives the oxime, m. p. 65–67°, and the 2,4-dinitro-phenylhydrazone, m. p. 149–150°. The latter derivative was identical with the 2,4-dinitro-phenylhydrazone of the natural substance in the infrared spectrum and the mixed melting point. From the above results, it is established that perillaketone is β-furyl isoamyl ketone.



(I)

Experimental

3-Furoyl chloride[3] 3-Furoic acid (25.0 g.) and thionyl chloride (50 cc.) were heated in benzene (160 cc.) for 9 hours. The solvent and an excess of thionyl chloride were evaporated and the residual liquid was distilled *in vacuo*. The acid chloride (16.2 g.) was obtained as a colorless liquid, b. p. 73–76°/46 mm.

β-Furyl isoamyl ketone (Perillaketone) To the Grignard solution, prepared from isoamyl bromide (30 g.), magnesium (4.9 g.) and absolute ether (80 cc.), dried cadmium chloride (19 g.) was added in portions under ice-cooling and the mixture was refluxed until a negative Gilman-Schulz test was given. Ether was evaporated and benzene (100 cc.) was added. A solution of 3-furoyl chloride (16.2 g.) in benzene (50 cc.) was rapidly added to the above cadmium diisoamyl solution at room temperature. The mixture was refluxed for 20 minutes and was decomposed with diluted hydrochloric acid under ice-cooling. The benzene layer was separated, washed with bicarbonate solution, dried and evaporated. Distillation of the residual liquid (17.0 g.) gave the crude ketone as a pale yellow liquid (8.5 g.); b. p. 73–75°/3 mm. and n_D^{27} 1.4685.

The crude product was treated with the Gigrard reagent P in the usual method. Distillation of the ketonic part gave the pure ketone as a color-

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[1] R. Goto, *J. Pharm. Soc. Japan*, **57**, 77 (1937).

[2] Y. Sebe, *J. Chem. Soc. Japan*, **64**, 1130 (1943).

[3] H. Gilman, R. Burtner, *J. Am. Chem Soc.*, **55**, 2903 (1933).

Table I

		B. P.	n_D	d	Oxime (m. p.)	2,4-Dinitrophenylhydrazone (m. p.)
β-Furyl isoamyl ketone		72—73°/3 mm	n_D^{17} 1.4741	d_4^{24} 0.9924	65—66°	149—150°
Perillaketone	Goto1)	196°	n_D^{20} 1.4781	d_{15}^{15} 0.9920	67°	—
	Sebe2)	95—97°/7 mm	n_D^{17} 1.4759	d_4^{17} 0.9897	66—67°	152—153°

less liquid; b. p. 72-73°/3 mm., n_D^{17} 1.4741 and d_4^{24} 0.9924. The substance gives a negative test with the Ehrlich reagent and shows a pale yellow color with acetic anhydride and sulfuric acid. The ketone is sensitive to oxygen and on standing becomes a reddish orange color.

IR-absorptions: 3.18, 3.42, 3.50, 6.00, 6.41, 6.63, 6.82, 7.20, 7.30-7.34, 7.78, 8.10, 8.32, 8.66, 9.25, 9.50, 9.77, 10.02, 10.78, 11.45, 12.30, 12.90 and 13.48 μ.

Oxime of β-furyl isoamyl ketone The ketone (2.1 g.), hydroxylamine hydrochloride (1.3 g.) and sodium acetate (2.5 g.) were treated in the usual method in diluted alcohol. The oily product (1.9 g.) solidified on standing in the ice-chest. The oxime crystallized from petroleum ether in colorless needles, m. p. 65-66°. Anal. Found: C, 66.52; H, 8.41; N, 8.03 %. Calcd. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73 %.

2,4-Dinitro-phenylhydrazone of β-furyl isoamyl ketone The ketone (0.3 g.) and 2,4-dinitro-phenylhydrazine (0.4 g.) precipitated reddish orange needles in the presence of sulfuric acid in alcohol. Recrystallizations of the needles gave the pure 2,4-dinitro-phenylhydrazone, m. p. 149-150°, which showed no depression on admixture with 2,4-dinitro-phenylhydrazone, m. p. 151-152°, of natural perillaketone. Anal. Found: C, 55.48; H, 5.20; N, 16.08 %. Calcd. for $C_{16}H_{18}N_4O_5$: C, 55.48; H, 5.24; N, 16.18 %.

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