A New Method of Preparing 2-Alkylbenzofuran from 2-Alkyl-3(2H)-benzofuranone

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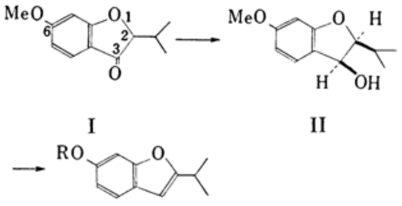
For the preparation of 2-alkylbenzofurans, two methods seem to be generally applicable, by the reduction of 2-alkyl-3(2*H*)-benzofuranone oxims followed by deamination[1], and by the dehydrogenation of 2, 3-dihydro-2-alkylbenzofurans[2]. However, neither method is entirely satisfactory because of their low yields and too many steps. In the case of the 2-isopropyl derivatives, they have been prepared from 2-acetyl derivatives by the Grignard reaction[3].

Now a new, easier method for the synthesis of general 2-alkylbenzofuran from 2-alkyl-3-(2*H*)-benzofuranone has been explored; the ketone was reduced with lithium aluminum hydride or with sodium borohydride to give 2, 3-dihydro-2-alkyl-3-benzofuranol, which was then readily converted into 2-alkylbenzofuran by dehydration.



I II

III R=Me
IV R=H

Reduction of 2-isopropyl-6-methoxy-3(2*H*)-benzofuranone (I), followed by subsequent treatment with acetic acid, furnished *cis*-2, 3-dihydro-2-isopropyl-6-methoxy-3-benzofuranol (II) in the form of colorless crystals with a sharp odor. The hydroxyl group of II seems to be cis to the isopropyl group, considering its formation procedure, the difficulty with which it forms nitrobenzoate, and the easiness with which it can be dehydrated. The distillation of II or the use of hydrochloric acid in the above-mentioned reduction of I readily furnished 2-isopropyl-6-methoxybenzofuran (III). The reflux of II with anhydrous pyridine hydrochloride furnished 6-hydroxy-2-isopropylbenzofuran (IV).

Experimental*

***cis*-2, 3-Dihydro-2-isopropyl-6-methoxy-3-benzofuranol (II).**—(*a*) *By Lithium Aluminum Hydride*.—A solution of 2-isopropyl-6-methoxy-3(2*H*)-benzofuranone[4] (I, m. p. 74∼75°C, IR: ν_{CO} 1675 cm^{-1} (KBr), 2 g.) in anhydrous ether (20 ml.) was stirred into a suspension of lithium aluminum hydride

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[1] R. Stoermer and W. König, *Ber.*, **39**, 492 (1906); P. Friedländer, ibid., **47**, 1919 (1914); B. Kamthong and A. Robertson, *J. Chem. Soc.*, **1939**, 933; K. Horváth, *Monatsh.*, **82**, 901 (1951).

[2] B. Klarmann, *J. Am. Chem. Soc.*, **73**, 4476 (1951); H. Bickel and H. Schmid, *Helv. Chim. Acta*, **36**, 664 (1953).

[3] A. Robertson, *J. Chem. Soc.*, **1949**, 2057; M. Miyano and M. Matsui, *Chem. Ber.*, **92**, 2487 (1959).

* Melting and boiling points are uncorrected.

[4] J. Arima and T. Okamoto, *J. Chem. Soc. Japan* (*Nippon Kwagaku Kwaishi*), **50**, 344 (1929); W. Bridge, A. J. Crocker, T. Cubin and A. Robertson, *J. Chem. Soc.*, **1937**, 1530.

(0.4 g.) in ether (80 ml.), and the mixture was then refluxed for one hour. The cooled mixture was acidified with dilute aqueous acetic acid, and the ether layer was separated and washed with dilute aqueous sodium hydroxide. The crystalline product obtained from the ethereal solution was recrystallized from petroleum benzine to give II in the form of colorless crystals; m. p., 108~109°C; yield, 1 g. (50%). IR: ν_{OH} 3220 cm^{-1} (KBr) or 3480 cm^{-1} ($CHCl_3$). Found: C, 69.24; H, 7.74. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%.

(*b*) *By Sodium Borohydride.*—A solution of sodium borohydride (0.5 g.) in ethanol (20 ml.) was slowly added to a solution of the ketone I (1 g.) in ethanol (30 ml.), and the mixture was heated at 65~70°C for 2 hr. In this reduction, the reaction temperature was important, for the starting material was recovered only when the temperature was lower. Most of the ethanol was removed in vacuo; the residue was acidified with dilute aqueous acetic acid and extracted with ether. The ethereal solution was washed with dilute aqueous sodium hydroxide, and the product was recrystallized from petroleum benzine; m. p., 107~109°C. Yield, 0.5 g. (50%).

2-Isopropyl-6-methoxybenzofuran (III).—Distillation of II in vacuo or treatment with dilute hydrochloric acid instead of acetic acid in the abovementioned reduction of I gave III as a colorless oil; b. p., 130~135°C/3 mmHg. Picrate: red crystals; m. p., 60~61°C (from ethanol). Found: N, 10.75. Calcd. for $C_{18}H_{17}O_9N_3$: N, 10.02%.

6-Hydroxy-2-isopropylbenzofuran (IV).—A mixture of II (0.3 g.) and anhydrous pyridine hydrochloride (1.5 g.) was refluxed for 20 min. on an oil-bath (220°C). The cooled product was treated with dilute hydrochloric acid and extracted with ether. The ethereal solution was extracted with dilute aqueous sodium hydroxide, and the product obtained by acidifying the alkaline solution was distilled in vacuo (b. p., 130°C/0.001 mmHg) and then crystallized from petroleum benzin to give IV in the form of colorless microcrystals; m. p., 75~76°C; yield, 0.1 g. The reported m. p. is 75~76°C(1). Found: C, 74.72; H, 7.03. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86%.

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