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Abstract

Full Text

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ALKYLATION OF 2-CHLOROANISOLE WITH PROPYLENE, BUTENE-2, AND CYCLOHEXENE IN THE PRESENCE OF $BF_3 \cdot H_3PO_4$

Alkylhaloanisoles, as is known, are compounds that are still not readily accessible, owing to the absence of simple methods for their synthesis. In one of our works it was shown that, in the alkylation of 4-chloroanisole with propylene, butene-2, and cyclohexene in the presence of the catalyst $BF_3 \cdot H_3PO_4$, mono- and dialkyl-4-chloroanisoles are formed with an overall yield, depending on the conditions, of 90 to 100% of theory. Developing studies in this direction, we investigated the reaction of 2-chloroanisole with propylene, butene-2, and cyclohexene in the presence of the same catalyst. The reaction was studied under the conditions that had been established as the most favorable for the alkylation of 4-chloroanisole. It was found that, in the alkylation of 2-chloroanisole with the indicated olefins, in contrast to 4-chloroanisole, only monoalkyl-2-chloroanisoles are obtained. Moreover, with propylene and butene-2 such compounds are 4-alkyl-2-chloroanisoles, which already during the first distillation of the alkylate distill within a range of 2° and are recovered almost without residue (the residue in the flask in the form of a brown resin is 0.2–0.4 g). The yield of these products is 96–97% of theory, i.e., somewhat higher than the overall yield of mono- and dialkyl-4-chloroanisoles. In the reaction with cyclohexene, two monocyclohexyl-2-chloroanisoles are formed: crystalline and liquid. The former, upon heating for many hours with HI or HBr, is demethylated to the corresponding cyclohexyl-2-chlorophenol, and it is assigned the structure of 4-cyclohexyl-2-chloroanisole. The liquid one is not demethylated under analogous conditions and does not crystallize at −20°. It is assumed that it is 6-cyclohexyl-2-chloroanisole. The relative content of the liquid isomer in the crystalline one is 5.1% (from 105.4 g of liquid, 5.4 g was isolated). The overall yield of the *o*- and *p*-isomers, depending on the conditions, was from 93 to 98%. They distill together at 138–142°/3 mm and likewise almost completely (the residue of brown resin in the flask is 0.4–0.6 g).

Experimental Part

2-Chloroanisole was obtained by diazotization of *o*-anisidine by analogy with the synthesis of 4-chlorotoluene ([1]). B.p. 66–67° at 2 mm, d_4^{20} 1.1927, n_D^{20} 1.5460.

Propylene, butene-2, cyclohexene, and the catalyst were obtained as previously ([2]). The reaction was carried out similarly to the alkylation of 4-bromophenol with olefins ([3]).

1. **Alkylation of 2-chloroanisole with propylene.**
   88 g of 2-chloroanisole, 7.0 g of $BF_3 \cdot H_3PO_4$, and 8.6 g of propylene (molar ratios 3 : 1 : 0.2) were heated for 2 hours at 60°; the mixture was left for 12 hours at room temperature, treated in the appropriate manner, and distilled. There were obtained 36.2 g, or 96% of the theoretical yield, of 4-isopropyl-2-chloroanisole (I), boiling at 91-92° at 3 mm and having n_D^{20} 1.5242, 56.5 g of unreacted 2-chloroanisole, and 0.4 g of residue in the distillation flask in the form of a brown resin. From 115.2 g of 2-chloro-

anisole, 10.6 g of $BF_3 \cdot H_3PO_4$ and 8.4 g of propylene (molar ratios 4 : 1 : 0.3) under analogous conditions gave 35.5 g, or 96.2% of theory, distilling at 93–94°/4 mm, 86.1 g of unchanged 2-chloroanisole, and 0.3 g of residue–resin.

4-Isopropyl-2-chloroanisole (I) is a colorless oily liquid of pleasant odor. On redistillation it has b.p. 91–92°/3 mm, d_4^{20} 1.0872, n_D^{20} 1.5245, MR_D found 51.92; calculated 51.28.

Found, %: Cl 19.17; 19.07

$C_{10}H_{13}OCl$. Calculated, %: Cl 19.21

4-Isopropyl-2-chlorophenol (II) was obtained in 77.8% yield by heating (I) with hydrobromic acid for 45 h. It is a colorless oily liquid. B.p. 70–71°/3 mm, d_4^{20} 1.1265, n_D^{20} 1.5336, MR_D found 47.02; calculated 46.55.

4-Isopropyl-2-chlorophenoxyacetic acid was obtained from (II) in 59.7% yield. It forms white lustrous plates. M.p. 72–73° (from petroleum ether).

2. Alkylation of 2-chloroanisole with butene-2. 85.6 g of 2-chloroanisole, 7.9 g of $BF_3 \cdot H_3PO_4$ and 10.7 g of butene-2 (molar ratios 3 : 1 : 0.2) were heated for 3.5 h at 60°; the reaction mass was left overnight at room temperature, worked up in the appropriate manner, and distilled. This gave 36.4 g, or 96.1% of the theoretical yield, of 4-sec.-butyl-2-chloroanisole (III), boiling at 99–101°/4 mm and having n_D^{20} 1.5225, 58 g of unreacted 2-chloroanisole, and 0.3 g of residue in the form of brown resin. From 114.8 g of 2-chloroanisole, 10.4 g of $BF_3 \cdot H_3PO_4$ and 11.5 g of butene-2 (molar ratios 4 : 1 : 0.3), at the same temperature and with a reaction time of 1 h 10 min, 39.5 g of (III), or 97% of the theoretical yield, were obtained; it distilled within 97–99°/3 mm, with 84.9 g of unreacted 2-chloroanisole and 0.2 g of residue in the flask in the form of resin.

4-sec.-Butyl-2-chloroanisole (III) is a colorless oily liquid with a faint anisole odor. B.p. 97–98°/2 mm, d_4^{20} 1.0700, n_D^{20} 1.5220, MR_D found 56.59; calculated 55.90.

Found, %: Cl 17.85; 17.64

$C_{11}H_{15}OCl$. Calculated, %: Cl 17.84

4-sec.-Butyl-2-chlorophenol (IV) was obtained in 76% yield by heating (III) with hydrobromic acid for 45 h. It is a colorless liquid with a faint phenolic odor. B.p. 82°/3 mm, d_4^{20} 1.1061, n_D^{20} 1.5292, MR_D found 51.45; calculated 51.28.

4-sec.-Butyl-2-chlorophenoxyacetic acid was obtained from (IV) in 53.3% yield. M.p. 84–85°.

3. Cycloalkylation of 2-chloroanisole with cyclohexene. The reaction was carried out as above. For each experiment, 0.1 mole of cyclohexene and the corresponding amounts of 2-chloroanisole and $BF_3 \cdot H_3PO_4$ were taken. The orthophosphoric acid was saturated with a 20–30% excess of boron fluoride. Cyclohexene was added over one hour, after which the mixture was stirred for 2 h and left overnight at room temperature. The most characteristic experiments are summarized in Table 1.

The products of cycloalkylation from all experiments, after standing for a week at room temperature, crystallized almost completely. From 105.4 g, 5.4 g of a liquid isomer were separated by suction under vacuum.

4-Cyclohexyl-2-chloroanisole (V) (crystalline isomer) forms white plates with m.p. 56° (from methyl alcohol).

Found, %: Cl 15.71; 15.61

$C_{13}H_{17}OCl$. Calculated, %: Cl 15.78

Table 1

Cycloalkylation of 2-chloroanisole with cyclohexene

Experiment no.	Molar ratios of chloroanisole, cyclohexene, and $BF_3 \cdot H_3PO_4$	Temp., °C ± 2°	4- and 6-cyclohexyl-2-chloroanisoles yield, g	4- and 6-cyclohexyl-2-chloroanisoles, % of theory	4- and 6-cyclohexyl-2-chloroanisoles boiling range, °C/mm	4- and 6-cyclohexyl-2-chloroanisoles n_D^{20}	Residue in flask, g
1	3 : 1 : 0.2	30	20.8	92.6	138–142/3	1.5474	0.6
2	3 : 1 : 0.3	60	21.0	93.5	139–142/3	1.5470	0.4
3	3 : 1 : 0.3	30	20.9	93.1	138–142/3	1.5475	0.5

Experiment no.	Molar ratios of chloroanisole, cyclohexene, and $BF_3 \cdot H_3PO_4$	Temp., °C ± 2°	4- and 6-cyclohexyl-2-chloroanisole yield, g	4- and 6-cyclohexyl-2-chloroanisoles, % of theory	4- and 6-cyclohexyl-2-chloroanisoles, boiling range, °C/mm	4- and 6-cyclohexyl-2-chloroanisoles, n_D^{20}	Residue in flask, g
4	3 : 1 : 0.3	20	20.7	92.2	138–142/3	1.5480	0.6
5	4 : 1 : 0.3	30	22.0	98.0	138–142/3	1.5475	0.4

4-Cyclohexyl-2-chlorophenol (VI) was obtained in 85.4% yield by heating (V) with hydrobromic acid for 45 h. It has b.p. 122–123°/3 mm, d_4^{20} 1.1494, n_D^{20} 1.5544, MR_D found 58.75; calculated 58.58. On standing it crystallizes. M.p. 39°. Literature data: b.p. 160.5°/12.5 mm, m.p. 41.5–42°, n_D^{20} 1.5578 (4); b.p. 134.5°/2 mm, m.p. 53° (5).

4-Cyclohexyl-2-chlorophenoxyacetic acid was obtained from (VI) in 74.5% yield. M.p. 124–125° (from petroleum ether).

6-Cyclohexyl-2-chloroanisole (VIII) (liquid isomer) has b.p. 124–126°/3 mm, d_4^{20} 1.1116, n_D^{20} 1.5410, MR_D found 63.53; calculated 62.94. On prolonged cooling to −20° it does not crystallize. When heated with hydrobromic acid for 90 h it is recovered practically quantitatively unchanged.

$C_{13}H_{17}OCl$.

Found, %: Cl 15.73
Calculated, %: Cl 15.78

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Note: Figure translations are in progress. See original paper for figures.