CATALYTIC ALKYLATION OF BENZOFURANS

I. ALKYLATION OF BENZOFURAN WITH tert-BUTYL CHLORIDE

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The alkylation of benzofuran with tert-butyl chloride in various solvents with a zinc chloride catalyst was studied. It was found that the alkylation proceeds primarily at the 3-position. The ratio of the 2- and 3-tert-butylbenzofurans is ~ 1:2 regardless of the nature of the solvent.

According to Brown's data [1], the center with the maximum electron density in the benzofuran molecule is the 2-position of the heterocyclic ring, and the formation of primarily 2-substituted benzofurans should be expected in nitration, sulfonation, and acylation reactions.

The scope of this work included a study of the alkylation of benzofuran with tert-butyl chloride in a static system in the presence of a zinc chloride catalyst. The alkylation was carried out in the presence of solvents of different nature (Table 1) at 60 deg C. The experiments indicated that a mixture of the isomeric 2- and 3-tert-butylbenzofurans is always formed in the alkylation.

The nature of the solvent used substantially affects the overall yield of the tert-butylbenzofurans. Thus, while the yield of the latter reaches 78% of the theoretical in n-hexane, alkylation was not observed in dioxane and dimethylformamide from 60 to 100 deg because of the formation of a coordination complex of the catalyst with the solvent. At the same time, the nature of the solvent does not change the ratio of the isomers formed, which is ~ 1:2 for all of the experiments; i.e., substitution at the 3-position of the heterocyclic ring predominates in all cases. Raising the temperature to 100 deg, by increasing the yield of alkylation products, equalizes the effect on it of the nature of the solvent. Changing the contact time with the catalyst does not substantially affect the isomer ratio (Table 2).

The results obtained and the properties of the alkylating agent and the catalyst make it possible to assume that the alkylation proceeds through the formation of an intermediate complex, viz., $\overset{(+)}{C}(CH_3)_3 \ldots \overset{(-)}{Zn}Cl_3$.

TABLE 1. Results of the Alkylation of Benzofuran with tert-Butyl Chloride in the Presence of Zinc Chloride

Solvent	Temperature, °C	Overall yield of alkylation products (% of the theoretical)	Catalysate composition, %						Ratio of 2- and 3-tert-butylbenzofurans
			benzofuran	2-tert-Butylbenzofuran	3-tert-Butylbenzofuran	2-n-Butylbenzofuran	phenol	unidentified substances	
n-Hexane	60	78	7	23	52	3	5	10	1 : 2,2
Nitrobenzene	60	67	33	25	42	—	—	—	1 : 1,7
Toluene	60	27	69	8	19	Traces	—	4	1 : 2,3
	100	63	28	22	41	Traces	—	9	1 : 1,9
Glacial acetic acid	60	20	77	6	14	Traces	—	2	1 : 2,3
	100	63	29	21	42	Traces	6	2	1 : 2

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TABLE 2. Effect of Contact Time on the Ratio of 2- and 3-tert-Butylbenzofurans*

Contact time, h	2-tert-Butyl benzofuran	3-tert-Butyl-benzofuran	Ratio of 2- and 3-butylbenzofurans
1	12	24	1 : 2
2	12	24	1 : 2
3	18	44	1 : 2,4
4	24	48	1 : 2
6	23	52	1 : 2,2

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* The experimental temperature was 60 deg, and n-hexane was the solvent.

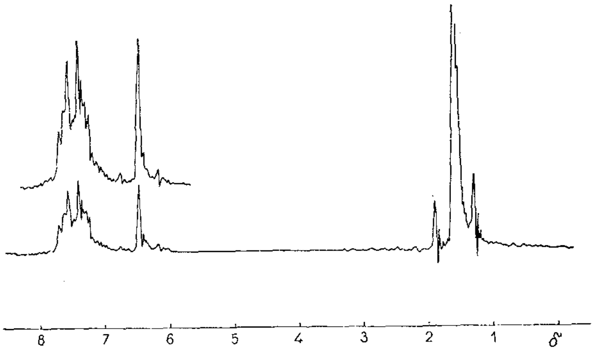

Fig. 1. PMR spectrum of 2-tert-butylbenzofuran.

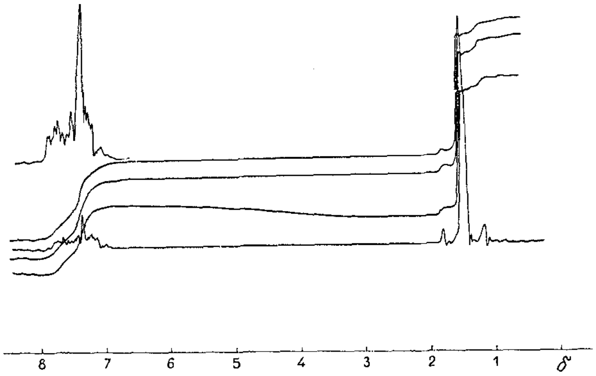

Fig. 2. PMR spectrum of 3-tert-butylbenzofuran.

The possibility of interconversions of the isomeric tert-butylbenzofurans was checked by special experiments with the individual isomers under the alkylation conditions (60 deg, n-hexane solvent, hydrogen chloride stream), as a result of which it was shown that isomerization does not occur. Also in favor of this conclusion are the data in Table 2.

The predominant formation of 3-tert-butylbenzofuran can be explained by partial deactivation of the 2-position in the benzofuran molecule due to weak interaction of the electron pair of the oxygen of the heterocycle with the zinc chloride molecule. It is extremely possible that the coordination complex formed in the process also creates steric hindrance at the 2-position.

EXPERIMENTAL

Benzofuran was alkylated under static conditions (flask with a stirrer and a reflux condenser) in absolute solvents. The molar ratio of benzofuran, tert-butyl chloride, and zinc chloride was 0.1:0.14:0.04. The reaction mass was washed free of hydrogen chloride, dried, and subjected to chromatographic analysis. The yields of the catalysates were 100%.

Chromatographic analysis of the catalysates was carried out with an LKhM-7A chromatograph with a thermal conductivity detector. The column was 3 m long and 3 mm in diameter, the phase was polyethylene glycol adipate on Chromosorb W-45/60, and the analytical temperature was 180 deg.

The mixture of 2- and 3-tert-butylbenzofurans formed in the alkylation was separated with a rectification column with an efficiency of 80 theoretical plates (the purity of the isomers was 97-98%) and with a preparative chromatograph

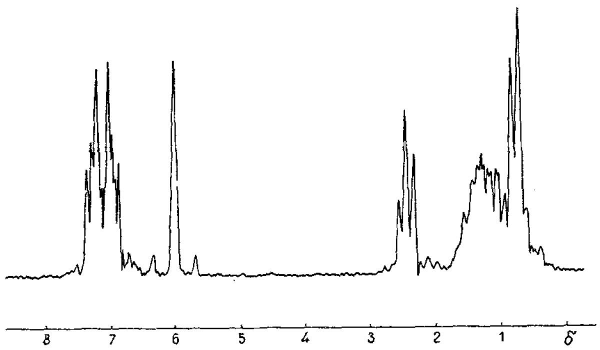

Fig. 3. PMR spectrum of 2-n-butylbenzofuran.

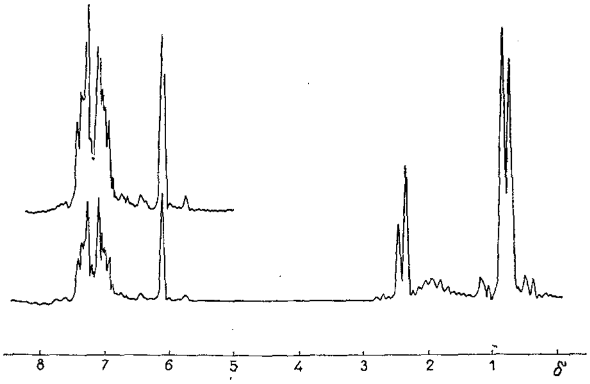

Fig. 4. PMR spectrum of 2-isobutylbenzofuran.

with a flame ionization detector. PEG-20000 was used as the phase (the column was 6 m long and 4 mm in diameter).

The 2-tert-butylbenzofuran obtained (100% purity) had bp 105-107 deg (15 mm), n_D^{20} 1.5300, and d_4^{20} 1.0334. The 3-tert-butylbenzofuran obtained (100% purity) had bp 108-109 deg (15 mm, n_D^{20} 1.5260, and d_4^{20} 1.0025. The structures of the isomers isolated were confirmed by PMR spectra (see Figs. 1 and 2).

The isomeric 2-butylbenzofurans, obtained by the reduction of corresponding ketones [2], were used to identify the other components of the catalysate. The 2-n-butylbenzofuran obtained had bp 127-128 deg (13 mm), n_D^{20} 1.5355, and d_4^{20} 0.9945 (see Fig. 3 for the PMR spectrum) (bp 126 deg (11 mm) and n_D^{20} 1.5358 [2]). The 2-isobutylbenzofuran obtained had bp 116-117 deg (13 mm), n_D^{20} 1.5319, and d_4^{20} 0.9928 (see Fig. 4 for the PMR spectrum). Found %: C 82.69, 82.72; H 8.0, 8.1; O 9.31, 9.18. $C_{12}H_{14}O$. Calc. %: C 82.76; H 8.04; O 9.2. This substance is described for the first time.

LITERATURE CITED

1. R. D. Brown and B. W. Coller, Austral. J. Chem., 12, 152 (1959).
2. N. P. Buu-Hoi, N. D. Xuong, and N. V. Bac, J. Chem. Soc., 173 (1964).