3. I. M. Skvortsov, N. A. Buntyakova, A. A. Stolyarchuk, and N. I. Ivanova, Khim.-farm. Zh., No. 5, 66 (1977).
4. V. Emerson, in: Organic Reactions [Russian translation], No. 5, Inostr. Lit., Moscow (1951), p. 347.
5. A. P. Terent'ev, R. A. Gracheva, and O. P. Shkurko, Zh. Obshch. Khim., 30, 3711 (1960).
6. A. A. Ponomarev, N. P. Maslennikova, and A. P. Kriven'ko, Zh. Obshch. Khim., 31, 958 (1961).
7. I. F. Bel'skii, Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 493 (1962).

SYNTHESIS AND TRANSFORMATIONS OF 2-BROMOMETHYL-3-BENZOYL-5-ACETOXYBENZOFURAN

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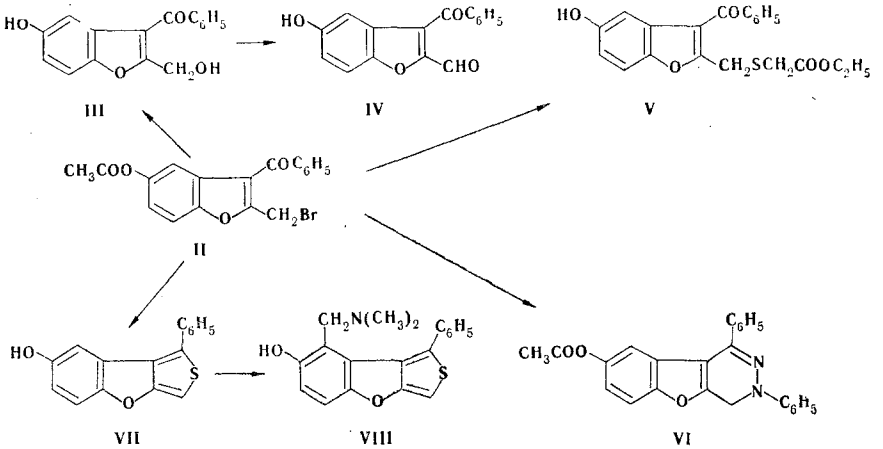
UDC 547.728.2'735'852.9.07:543.422.51

2-Bromomethyl-3-benzoyl-5-acetoxybenzofuran was synthesized, and its reaction with nucleophilic reagents was studied. Various benzofuran derivatives, as well as condensed systems that include a benzofuran ring, were obtained. The structures of the synthesized compounds were proved by PMR and mass spectrometry.

We have previously shown that when electrophilic substitution reactions with 5- and 6-hydroxybenzofurans are carried out, the substituents are incorporated primarily in the benzene ring, whereas substitution in the benzene ring is excluded in the action of electrophilic agents on the corresponding acetoxy derivatives of benzofurans, and the substituent is incorporated only in the furan ring or in the side chain of the benzofuran derivative [1-3]. These investigations, which create new prospects from the point of view of the synthesis of various benzofuran derivatives, have undergone further development in the present research.

We have found that 2-methyl-3-benzoyl-5-acetoxybenzofuran (I) is converted to 2-bromomethyl-3-benzoyl-5-acetoxybenzofuran (II) by bromination in nonaqueous solutions with N-bromosuccinimide (NBS) in the presence of benzoyl peroxide and with illumination. We also showed that II is a convenient starting compound for the synthesis of both benzofuran derivatives and condensed systems that include a benzofuran ring. The bromine atom is replaced by a hydroxy group by the action of water on II. The resulting hydroxymethyl-3-benzoyl-5-hydroxybenzofuran (III) was oxidized with the chromium trioxide—pyridine complex to 2-formyl-3-benzoyl-5-hydroxybenzofuran (IV). Bromomethyl derivative II is converted to ethyl 3-benzoyl-5-hydroxybenzofuranyl-2-methylthioglycolate (V) in 61% yield by the action of ethyl trioglycolate. Compound II reacts with N-phenylhydrazine to give 1,3-diphenyl-4H-8-acetoxypyridazino[5,4-b]-benzofuran (VI), whereas 1-phenyl-7-hydroxythieno[3,4-b]benzofuran (VII) is formed when it is treated with thioacetamide. We established that in the case of aminomethylation of VII the



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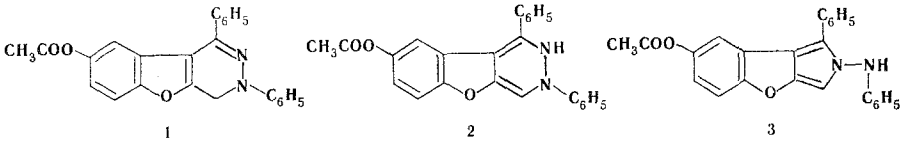
 0009-3122/83/1902-0144$07.50

aminomethyl group enters the 8 position of the molecule rather than the thiophene ring to give 1-phenyl-7-hydroxy-8-dimethylaminomethylthieno[3,4-b]benzofuran (VIII) hydrochloride.

We used PMR and mass spectroscopy to establish the structures of VI and VII.

An intense molecular-ion peak (m/z 382) and an $[M-H]^+$ ion peak of almost equal intensity are observed in the mass spectrum of VI. Elimination of an acetyl group is another favorable pathway for the fragmentation of $M^{+\cdot}$. The spectrum does not contain peaks of $[PhNH]^+$ and $[M-PhNH]^+$ ions, which should be expected in the case of the formation of structure 3. These data are in good agreement with the assumption that product VI has the 2-H- or 4-H-pyridazinobenzofuran (1 or 2) structure:



1 2 3

The subsequent fragmentation also confirms the proposed structures. Peaks of $[PhNCH]^+$, $[Ph-N=NH]^+$, $[M-COCH_3, -PhNCH_2]^+$, $[M-COCH_3, -PhNCH]^+$, and $[M-COCH_3, -PhCN]^+$ ions are observed in the spectrum. Of the other fragmentation pathways, one should note the elimination of a $CH_3COO^{\cdot}$ particle or the successive elimination of $CH_3CO^{\cdot}$ and CO from the molecular ion; the resulting fragments (m/z 323 and 311) subsequently split out 105 amu ($PhNCH_2$ or PnH_2).

In addition to a multiplet at δ 7.05-7.80 ppm, which is related to the aromatic protons, and a singlet at δ 2.25 ppm, which is related to the acetoxy group, a singlet of a methylene group (δ 5.07 ppm) is observed in the PMR spectrum of VI, and this constitutes evidence in favor of structure 1.

The most intense peak in the spectrum corresponds to the molecular ion of VII (m/z 266). The high stability of the molecular ion is in agreement with the aromatic character of 1-phenyl-7-hydroxythieno[3,4-b]benzofuran (VII). Low-intensity peaks of $[M-HCO]^+$, $[M-S]^+$, $[M-SCH]^+$, $[M-PhC=C]^+$, and $[C_6H_5CS]^+$ ions, the formation of which is in good agreement with the structure proposed for this compound, are observed in the spectrum of VII.

EXPERIMENTAL

The mass spectra were obtained with a Varian MAT-112 spectrometer at an ionizing voltage of 70 eV and an ionization-chamber temperature of 180°C with direct introduction of the samples into the ion source.

2-Methyl-3-benzoyl-5-acetoxybenzofuran (I). A 1-g (4 mmole) sample of 2-methyl-3-benzoyl-5-hydroxybenzofuran was refluxed for 3 h with 5 ml of acetic anhydride, after which the mixture was poured into water, and the liberated oil was extracted with chloroform. The chloroform layer was separated and chromatographed with a column filled with KSK silica gel by elution with chloroform. The first fraction was collected and worked up to give 1.12 g (95.2%) of a product with mp 74-76°C. Found: C 73.0; H 4.5%. $C_{18}H_{14}O_4$. Calculated: C 73.4; H 4.8%.

2-Bromomethyl-3-benzoyl-5-acetoxybenzofuran (II). A solution of 1.5 g (4 mmole) of I in 15 ml of carbon tetrachloride was refluxed for 5 h with 0.91 g (5.1 mmole) of N-bromosuccinimide (NBS) with illumination and in the presence of benzoyl peroxide. The precipitated succinimide was removed by filtration, and the carbon tetrachloride was removed by vacuum distillation. Compound II was subjected, without additional purification, to further transformations.

2-Hydroxymethyl-3-benzoyl-5-hydroxybenzofuran (III). A solution of 4.5 g (12 mmole) of II in 55 ml of dioxane and 25 ml of water was refluxed for 18 h, after which the solvents were removed by distillation, and the residue was chromatographed with a column filled with KSK silica gel by elution with chloroform. The second fraction was collected and worked up to give 1.45 g (45%) of a product with mp 147-148°C. Found: C 71.7; H 4.9%; M^+ 268. $C_{16}H_{12}O_4$. Calculated: C 71.6; H 4.5%; M 268.

2-Formyl-3-benzoyl-5-hydroxybenzofuran (IV). A solution of 1 g (3.7 mmole) of III in 5 ml of pyridine was added to the complex prepared from 8 ml of pyridine and 0.8 g of chromium trioxide. The next day, the reaction mixture was diluted with 10% hydrochloric acid, and the resinous precipitate was extracted with chloroform. The chloroform was removed by distillation, and the residue was recrystallized from methanol to give 0.21 g (21.2%) of a product with mp 191-192°C. Found: C 71.7; H 4.0%. $C_{16}H_{10}O_4$. Calculated: C 72.1; H 3.8%.

Ethyl 3-Benzoyl-5-hydroxybenzofuranyl-2-methylthioglycolate (V). A 1.32-ml (12 mmole) sample of ethyl thioglycolate and a solution of 4.5 g (12 mmole) of II in 20 ml of ethanol were added successively to a solution of sodium ethoxide (obtained from 0.28 g of sodium) in 30 ml of ethanol. After 3 days, half the volume of alcohol was removed by distillation, 4 ml of concentrated hydrochloric acid was added to the concentrate, and the mixture was refluxed for 1 h. The solvent was removed by distillation, and the residue was recrystallized to give 2.7 g (61%) of a product with mp 77-78°C (from ethyl acetate–hexane). Found: S 8.3%; M^+ 370. $C_{20}H_{18}SO_5$. Calculated: S 8.6%; M 370.

1,3-Diphenyl-4H-8-acetoxypyridazino[5,4-b]benzofuran (VI). A 2.36-ml (24 mmole) sample of N-phenylhydrazine was added at room temperature to a solution of 4.5 g (12 mmole) of II in 20 ml of ethanol, and the resulting precipitate was separated and washed on the filter with alcohol to give 3.4 g (74.7%) of a product with mp 180°C (dec., from ethyl acetate). Found: C 75.3; H 4.7; N 7.1%. $C_{24}H_{18}N_2O_3$. Calculated: C 75.4; H 4.7; N 7.3%.

1-Phenyl-7-hydroxythieno[3,4-b]benzofuran (VII). A solution of 4.5 g (12 mmole) of II in 40 ml of ethanol was refluxed for 3 h with 0.9 g (12 mmole) of thioacetamide, after which the alcohol was removed by distillation, and the residue was recrystallized from benzene–heptane to give 2 g (63.4%) of a product with mp 170-171°C. Found: C 72.1; H 3.8; S 12.0%. $C_{16}H_{10}SO_2$. Calculated: C 72.2; H 3.8; S 12.0%.

1-Phenyl-7-hydroxy-8-dimethylaminomethylthieno[3,4-b]benzofuran (VIII) Hydrochloride. A solution of 1 g (3.8 mmole) of VII in 20 ml of dioxane was refluxed for 3 h with 3 ml of bis-(dimethylamino)methane, after which the solvent and excess amine were removed by vacuum distillation, and the residue was dissolved in ether. The ether solution was neutralized with an ether solution of hydrogen chloride, and the precipitate was removed by filtration to give 0.7 g (51.8%) of a product with mp 192-193°C (from alcohol). PMR spectrum: 6.65 ppm (s, 3-H). Found: C 63.3; H 5.2; Cl 9.7%. $C_{19}H_{18}ClNO_2S$. Calculated: C 63.4; H 5.0; Cl 9.8%.

LITERATURE CITED

1. A. N. Grinev, S. A. Zotova, and T. F. Vlasova, Khim. Geterotsikl. Soedin., No. 3, 311 (1976).
2. F. A. Trofimov, N. G. Tsyshkova, and A. N. Grinev, Khim. Geterotsikl. Soedin., No. 3, 308 (1973).
3. A. N. Grinev, S. A. Zotova, A. A. Stolyarchuk, P. P. Gaevoi, and V. V. Matsak, Khim.-farm. Zh., No. 1, 51 (1979).

STRUCTURE AND RING-CHAIN TAUTOMERISM OF 3-(1-HYDROXY-4-BROMO-2-NAPHTHYL)PROPENAL

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UDC 547.652.9'655.1.6'816.07:541.62:543.422

The previously undescribed 3-(1-hydroxy-4-bromo-2-naphthyl)propenal was synthesized. This aldehyde exists primarily in the form of the cyclic 2H-chromene tautomer in the crystalline state, in solutions in nonpolar solvents, and in acetonitrile, ethanol, and acetone. Ring-chain tautomeric equilibrium between the 2H-chromene and quinoid structures is observed in dimethyl sulfoxide.

Previous studies of the electronic, vibrational, and PMR spectra of 3-(2-hydroxy-1-naphthyl)propenal [1] and 3-(1-hydroxy-4-methyl-2-naphthyl)propenal [2] have made it possible to establish that annelation of an additional benzene ring to the benzene ring of 2-hydroxycinnamaldehyde in the 5,6 and 3,4 positions shifts the benzenoid–quinoid equilibrium significantly to favor the quinoid tautomer, which promotes realization of the cyclic 2H-chromene structure in the crystalline state and in solutions in nonpolar solvents. Ring-chain tautomeric equilibrium between the 2H-chromene and chain (quinoid or benzenoid) forms is observed in polar solvents for these aldehydes; the percentage of the chain form increases substantially

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 181-184, February, 1983. Original article submitted February 22, 1982.

0009-3122/83/1902-0146$07.50