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# Polybromoaromatic Compounds: XI.* Reactions of 2,3,4,5,6-Pentabromobenzyl Bromide with Alcohols and Alkali Metal Alkoxides

**V. N. Shishkin[1], S. S. Vakaeva[1], and K. P. Butin[2]**

[1] *Ogarev Mordovian State University, ul. Bol'shevistskaya 68, Saransk, 430000 Russia*

[2] *Lomonosov Moscow State University, Moscow, Russia*

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**Abstract**—2,3,4,5,6-Pentabromobenzyl bromide reacts with primary and secondary alcohols and also with alkali metal alkoxides derived from primary alcohols to form the corresponding pentabromobenzyl ethers in high yields. In the reactions with secondary alkoxides, considerable amounts of bis(2,3,4,5,6-pentabromobenzyl) ether are formed.

Benzyl systems $PhCH_2X$ exhibit specific behavior in nucleophilic substitution reactions, often giving rise to nonlinear Hammett dependences. In due time, this gave grounds to the discussion whether the $S_N1$ mechanism changes to $S_N2$ gradually or both these operate simultaneously (a part of molecules react by the $S_N1$ mechanism, and the other part, by $S_N2$, their contributions depending on the substituent nature) [2, 3]. In this connection, interesting substrates are pentabromobenzyl derivatives. On the one hand, bromine atoms (as π-donors) in the *ortho* and *para* positions are capable of stabilizing polybromobenzyl cation; on the other hand, they are σ-acceptor substituents which destabilize cationic species. From the synthetic viewpoint, 2,3,4,5,6-pentabromobenzyl bromide (**I**) is a readily accessible reagent which is widely used for preparation of various functional derivatives containing a pentabromophenyl moiety, e.g., alcohols, ethers, esters, ketones, amines, etc. [4–10], including practically important ones [7–15].

In the present work we studied the behavior of pentabromobenzyl bromide (**I**) in reactions with alcohols and alkali metal alkoxides. The reactions of **I** with excess alcohols were carried out by heating at the boiling point until the initial bromide disappeared (TLC, Silufol plates, eluent toluene or petroleum ether; Table 1). As a result, the corresponding ethers were formed in high yields (runs nos. 1–5 in Table 1), indicating a very high mobility of the bromine atom in the bromomethyl group. When the reactions were carried out in aqueous–alcoholic mixtures (runs nos. 7 and 8; Table 1), 2,3,4,5,6-pentabromobenzyl alcohol (**II**) was also formed, and the reaction rate increased in the presence of water (cf. runs nos. 1 and 7; Table 1). These data suggest a considerable contribution of the $S_N1$ mechanism. An additional support comes from the fact that the reaction of **I** with 1.5 equiv of NaOH in 96% ethanol gives 2,3,4,5,6-pentabromobenzyl ethyl ether **III** as the major product, whereas alcohol **II** is formed in trace amounts.

The reactions of **I** with ethanol, 1-butanol, and 2-methyl-1-propanol are complete in 7–28 h, the reactions with 2-propanol and 2-butanol take 60–65 h, and with 2-methyl-2-propanol no reaction occurred even on heating for 100 h under reflux. These data indicate considerable steric hindrances to reactions with secondary and especially tertiary alcohols.

Bromide **I** reacts with alkali metal alkoxides derived from primary alcohols (runs nos. 1, 3, 4; Table 2) to give the corresponding ethyl, butyl, and isobutyl ethers (**III**–**V**) in high yields. However, in the reactions of **I** with *i*-PrONa and *s*-BuONa, apart from isopropyl 2,3,4,5,6-pentabromobenzyl ether (**VI**) and *s*-butyl 2,3,4,5,6-pentabromobenzyl ether (**VII**), respectively, up to 10% of a poorly soluble product was formed (runs nos. 2, 5; Table 2). Its melting point is 314–315°C, and it is the major product of the reaction of **I** with *t*-BuOK (runs nos. 6, 7; Table 2). The IR spectrum of this product contained a strong absorption band at 1100 $cm^{-1}$, which is typical of C–O

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**Table 1.** Reactions of 2,3,4,5,6-pentabromobenzyl bromide (**I**) with alcohols

| Run no. | ROH | Temperature °C (time, h) | Product (yield, %) | mp, °C |
|---|---|---|---|---|
| 1 | EtOH | 78 (28) | $C_6Br_5CH_2OEt$ (>98) | 124–125 |
| 2 | *i*-PrOH | 82 (60) | $C_6Br_5CH_2OPr$-i (>98) | 91–92 |
| 3 | BuOH | 112 (7.5) | $C_6Br_5CH_2OBu$ (88) | 71–72 |
| 4 | *i*-BuOH | 107 (22) | $C_6Br_5CH_2OBu$-i (>98) | 86–87 |
| 5 | *s*-BuOH | 98 (65) | $C_6Br_5CH_2OBu$-s (89) | 68–69 |
| 6 | *t*-BuOH | 82 (100) | – | – |
| 7 | Aqueous EtOH[a] | 78 (15.5) | $C_6Br_5CH_2OEt$ (94),[b] $C_6Br_5CH_2OH$ (6)[b] | – |
| 8 | Aqueous BuOH[c] | 92 (16) | $C_6Br_5CH_2OBu$ (89),[b] $C_6Br_5CH_2OH$ (11)[b] | – |

[a] 9 mol % of $H_2O$.
[b] Composition of the reaction mixture (mol %; GLC data).
[c] 21 mol % of $H_2O$.

bond vibrations in pentabromobenzyl ethers (see Experimental). We presumed that the product is bis-(2,3,4,5,6-pentabromobenzyl) ether (**VIII**). Its structure was proved by independent synthesis of ether **VIII** by reaction of benzyl bromide **I** with sodium pentabromophenylmethanolate in THF (run no. 8; Table 2). It should be noted that bromide **I** failed to react with $C_6Br_5CH_2ONa$ in dioxane even on heating for 10 h at 100°C. Likewise, no reaction occurred between pentabromobenzyl alcohol and compound **I** in dioxane in the presence of solid sodium ethoxide. A possible reason is that sodium alkoxides are insoluble in dioxane: Bromide **I** failed to react with EtONa in this solvent. We obtained ether **VIII** in a low yield (14%) by reaction of compound **I** with pentabromobenzyl alcohol in the presence of sodium ethoxide using a dioxane–ethanol mixture as solvent (run no. 9; Table 2).

The formation of ether **VIII** may be explained in terms of the reaction sequence given below, which includes cleavage of sterically hindered ethers by the action of alkoxides.

$$C_6Br_5CH_2Br \xrightarrow{RO^-} C_6Br_5CH_2OR$$
**I**

$$\xrightarrow{RO^-} C_6Br_5CH_2O^- \xrightarrow{\mathbf{I}} (C_6Br_5CH_2)_2O$$
**VIII**

R = *i*-Pr, *s*-Bu, *t*-Bu.

This scheme was confirmed by special experiments. Heating of ether **VI** with sodium isopropoxide in 2-propanol under reflux for 2 h resulted in formation of alcohol **II**. On the other hand, in the reaction of ethyl ether **III** with sodium ethoxide in ethanol under analogous conditions traces of alcohol **II** were detected only after heating of the mixture for 6 h.

## EXPERIMENTAL

The IR spectra were recorded on a UR-20 instrument in mineral oil. The $^1H$ NMR spectra were obtained on Tesla BS-467 (60 MHz) and Bruker AC-200 (200 MHz) spectrometers in $CCl_4$ or $CDCl_3$ using HMDS as internal reference. The purity of the initial compounds and reaction products was checked by GLC. All individual compounds contained no less than 97.5–98.5% of the main substance. GLC analysis was performed on a Chrom-42 chromatograph with a thermoionic detector; glass columns, $3000 \times 3.5$ and $1500 \times 3.5$ mm; stationary phase 3% OV-17 on Chromaton N-Super (0.16–0.20 mm); oven temperature 220–260°C; carrier gas nitrogen. Silufol UV-254 plates were used for TLC analysis; eluent toluene or petroleum ether; development with iodine vapor or UV light.

2,3,4,5,6-Pentabromobenzyl bromide (**I**) was synthesized by the procedure reported in [4].

**2,3,4,5,6-Pentabromobenzyl ethers III–VII.** *a*. A mixture of 1–4 mmol of pentabromobenzyl bromide **I** and 100 ml of the corresponding alcohol was heated under reflux until bromide **I** disappeared (7.5–65 h, TLC). The mixture was diluted with water, and the precipitate was filtered off, washed with water, dried, and recrystallized from ethanol. Ethers **III**–**VII** were thus obtained.

**Table 2.** Reactions of 2,3,4,5,6-pentabromobenzyl bromide (**I**) with alkali metal alkoxides

| Run no. | ROMe (solvent) | Molar ratio $C_6Br_5CH_2Br$ : ROMe | Temperature, °C (time, h) | Product (yield, %) | mp, °C |
|---|---|---|---|---|---|
| 1 | EtONa (EtOH) | 1 : 1.75 | 78 (2) | **III** (>98) | 124–125 |
| 2 | *i*-PrONa (*i*-PrOH) | 1 : 1.17 | 82 (2) | **VI** (78.8), **VIII** (3.2) | 91–92 (**VI**), 314–315 (**VIII**) |
| 3 | BuONa (BuOH) | 1 : 1.2 | 117 (2) | **IV** (76) | 70–72 |
| 4 | *i*-BuONa (*i*-BuOH) | 1 : 1.4 | 107 (2.5) | **V** (95) | 86–87 |
| 5 | *s*-BuONa (*s*-BuOH) | 1 : 1.4 | 98 (2.5) | **VII** (78), **VIII** (9.8) | 68–69 (**VII**), 314–315 (**VIII**) |
| 6 | *t*-BuOK (*t*-BuOH) | 1 : 1.4 | 82 (4.5) | **II** (9.4), **VIII** (73) | 314–315 (**VIII**) |
| 7 | *t*-BuOK (THF) | 1 : 2 | 65 (5) | **VIII** (85) | 314–315 |
| 8 | $C_6Br_5CH_2ONa$ (THF) | 1 : 1 | 65 (5) | **VIII** (78) | 314–315 |
| 9 | $C_6Br_5CH_2OH$, EtONa (dioxane, EtOH) | 1 : 1 : 1.5 | 100 (6) | **III** (86), **VIII** (14) | 124–125 (**III**), 314–315 (**VIII**) |

**Table 3.** $^1$H NMR and IR spectra and elemental analyses of alkyl pentabromobenzyl ethers **III**–**VII**

| Comp. no. | $^1$H NMR spectrum, δ, ppm | IR spectrum, ν, $cm^{-1}$ | Found, % | | Formula | Calculated, % | |
|---|---|---|---|---|---|---|---|
| | | | C | H | | C | H |
| **III** | (60 MHz, $CCl_4$), 1.17 t (3H, Me, *J* = 7.2 Hz), 3.37 q (2H, $CH_2$, *J* = 7.2 Hz), 4.83 s (2H, $CH_2C_6Br_5$) | 1335 m, 1260 w, 1200 m, 1100 s, 1035 w, 1000 w, 890 w | 20.35 | 1.14 | $C_9H_7Br_5O$ | 20.58 | 1.33 |
| **IV** | (200 MHz, $CDCl_3$), 0.93 t (3H, Me, *J* = 7.3 Hz), 1.27–1.69 m [4H, $(CH_2)_2$], 3.57 t (2H, $CH_2$, *J* = 6.2 Hz), 4.98 s (2H, $CH_2C_6Br_5$) | 1660–1740 w, 1345 m, 1260–1280 br.w, 1110 s, 1020 w | 23.60 | 2.10 | $C_{11}H_{11}Br_5O$ | 23.65 | 1.98 |
| **V** | (200 MHz, $CDCl_3$), 0.93 d (6H, 2Me, *J* = 6.5 Hz, 1.82–1.99 m (1H, CH), 3.32 d (2H, $CH_2$, *J* = 6.9 Hz), 4.98 s (2H, $CH_2C_6Br_5$) | 1640–1740 br.w, 1340 m, 1270 w, 1200 m, 1110 s, 1070 w, 1010 m | 23.48 | 1.93 | $C_{11}H_{11}Br_5O$ | 23.65 | 1.98 |
| **VI** | (60 MHz, $CCl_4$), 1.10 d (6H, 2Me, *J* = 6.5 Hz), 3.50–3.87 m (1H, CH), 4.83 s (2H, $CH_2C_6Br_5$) | 1315 s, 1225 m, 1115 s, 1070 s, 1050 s, 1000 m, 915 m, 830 w | 22.38 | 1.73 | $C_{10}H_9Br_5O$ | 22.05 | 1.67 |
| **VII** | (200 MHz, $CDCl_3$), 0.95 t (3H, Me, *J* = 7.3 Hz), 1.24 d (3H, Me, *J* = 6.2 Hz), 1.40–1.70 m (2H, $CH_2$), 3.43–3.60 m (1H, CH), 4.98 m (2H, $CH_2C_6Br_5$, *AA′* system, $J_{AA'}$ = 10.1 Hz, $\Delta\nu_{AA'}$ = 16.4 Hz) | 1620–1740 br.w, 1335 s, 1245 w, 1200 w, 1180 w, 1145 m, 1090 s, 1030 w, 1010 w, 980 w, 925 w | 23.78 | 1.83 | $C_{11}H_{11}Br_5O$ | 23.65 | 1.98 |

*b*. Metallic sodium, 10–20 mmol, was dissolved in 100 ml of anhydrous alcohol, 8–9 mmol of bromide **I** was added, and the mixture was heated for 2–2.5 h under reflux. It was then treated with water, and the precipitate was filtered off, washed with water, and dried in air. The crude product was recrystallized from the corresponding alcohol. The undissolved material was washed by hot dioxane (2 × 25 ml) and dried to obtain bis(2,3,4,5,6-pentabromobenzyl) ether (**VIII**). The reaction conditions and yields and melting points of the products are given in Tables 1 (method *a*) and 2 (method *b*). Table 3 contains the elemental analyses and spectral parameters of ethers **III**–**VII**.

**Bis(2,3,4,5,6-pentabromobenzyl) ether (VIII).** *a*. A mixture of 50 ml of anhydrous THF, 1 g (1.99 mmol) of pentabromobenzyl alcohol **II**, and 0.07 g (3.14 mmol) of metallic sodium was heated for 0.5 h under stirring. Bromide **I**, 1.13 g (2 mmol), was then added, and the mixture was heated for 5 h under reflux while stirring. The mixture was treated with water, and the precipitate was filtered off, washed with water on a filter, and dried in air. The product was washed with hot dioxane to remove impurities. Yield 0.91 g (46%), mp 314–315°C. IR spectrum, ν, $cm^{-1}$: 1650–1730 br.w, 1340 s, 1270 m, 1180 m, 1077 s, 1000 s, 713 m, 604 w, 547 w. Found, %: C 17.22; H 0.54; Br 79.49. $C_{14}H_4Br_{10}O$. Calculated, %: C 17.03; H 0.41; Br 80.94.

*b*. Potassium *tert*-butoxide, 1.38 g (12.3 mmol), was dissolved in 80 ml of anhydrous *tert*-butyl alcohol on heating, 5 g (8.84 mmol) of bromide **I** was added, and the mixture was heated for 5 h while stirring and treated with water. The precipitate was filtered off, washed with water, and dried in air. The product was washed with hot dioxane to remove alcohol **II**. Yield of **VIII** 3 g (73%). From the dioxane washings we isolated 0.97 g (9.4%) of pentabromobenzyl alcohol **II**.

*c*. Bromide **I**, 2 g (3.54 mmol), was added to a mixture of 0.4 g (3.57 mmol) of potassium *tert*-butoxide and 65 ml of anhydrous THF. The mixture was heated under reflux for 5 h (while stirring) and treated with water, and the precipitate was filtered off, washed with water and hot dioxane, and dried. Yield of **VIII** 1.15 g (65.7%).

*d*. A mixture of 60 ml of anhydrous dioxane, 0.2 g (2.94 mmol) of sodium ethoxide, and 3 ml of ethanol (which was added to solubilize sodium ethoxide) was heated to the boiling point (under stirring), and 1 g (2 mmol) of pentabromobenzyl alcohol **II** was added. After 10 min, 1.13 g (2 mmol) of benzyl bromide **I** was added, and the mixture was refluxed for 6 h. It was treated with cold water (~500 ml), and the precipitate was filtered off, washed with water on a filter, and dried in air. The crude product was extracted with hot dioxane (3 × 50 ml), and the undissolved material was filtered off and dried. We thus isolated 0.28 g (14%) of ether **VIII**. The extract was diluted with water to isolate 1.12 g (86%) of ether **III**.

**Cleavage of ethers III and VI by the action of sodium alkoxides.** Metallic sodium, 0.2 g (8.7 mmol), was dissolved in 55 ml of the corresponding anhydrous alcohol, 3.77 mmol of ether **III** or **VI** was added, and the mixture was refluxed for 6 h. Every 2 h, a sample was withdrawn and treated with cold water. The precipitate was filtered off, washed with water, dried, and analyzed by GLC and TLC.

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