ISSN 1070-4280, Russian Journal of Organic Chemistry, 2012, Vol. 48, No. 8, pp. 1062–1070. © Pleiades Publishing, Ltd., 2012.
Original Russian Text © M.V. Fadin, I.V. Tarasova, V.A. Vasin, V.N. Shishkin, 2012, published in Zhurnal Organicheskoi Khimii, 2012, Vol. 48, No. 8, pp. 1066–1074.

Products of Reaction between Tetrabromo-Substituted *ortho*- and *para*-Hydroxybenzoic Acids and Sodium Nitrite in CH_3COOH

M. V. Fadin, I. V. Tarasova, V. A. Vasin, and V. N. Shishkin†

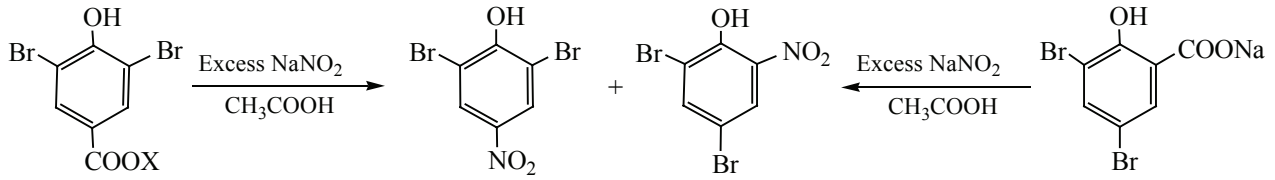
Ogarev Mordovian State University, Saransk, 430005 Russia
e-mail: orgchem@mrsu.ru

Received March 21, 2012

Abstract—The reaction of 2,3,5,6-tetrabromo-4-hydroxybenzoic acid with a 10-fold excess of $NaNO_2$ in the glacial acetic acid at 20°C affords tetrabromonitrosophenols whose further transformations under the reaction conditions leads to the formation of a mixture of 2,4,5,6-tetrabromo-*p*-quinone diazide and tetrabromo-*p*- and -*o*-nitrophenols in the molar ratio 37 : 2 : 1. Under similar conditions the 3,4,5,6-tetrabromo-2-hydroxybenzoic acid is converted into a mixture of 3,4,5,6-tetrabromo-*o*-quinone diazide with the same nitrophenols in the ratio 13 : 1 : 3. The reaction of sodium 2,3,5,6-tetrabromo-4-hydroxy-benzoate with $NaNO_2$ in dilute acetic acid resulted in a quantitative yield of tetrabromo-*p*-quinone monooxime.

DOI: 10.1134/S1070428012080064

It was established in [1] that dibromo-substituted *p*- and *o*-hydroxybenzoic acids **I** and **II** and/or their sodium salts reacted at 20°C with excess of $NaNO_2$ in the glacial acetic acid giving products of oxidative nitrosodecarboxylation, a mixture of isomeric dibromo-*p*- and -*o*-nitrophenols **III, IV**. The reaction proceeds along the mechanism of electrophilic aromatic *ipso*-substitution involving the nitrosonium cation generated from sodium nitrate by the action of CH_3COOH. The result of the reaction is due to the intra- and intermolecular rearrangements of the intermediate *ipso*-nitrosocomplexes.



Ia, Ib **III** **IV** **II**

X = H (**a**), Na (**b**).

Presuming that a similar rearrangement may be of a general character in the reactions of nitrosodecarboxylation of brominated hydroxybenzoic acids and that the reactions proper are synthetically valuable for the preparation of diverse difficultly available functionalized polybrominated derivatives we investigated the transformations of tetrabromo-substituted *p*- and *o*-hydroxybenzoic acids **V, VI** and some other brominated hydroxybenzoic acids in acetic acid in the presence of $NaNO_2$ under various conditions.

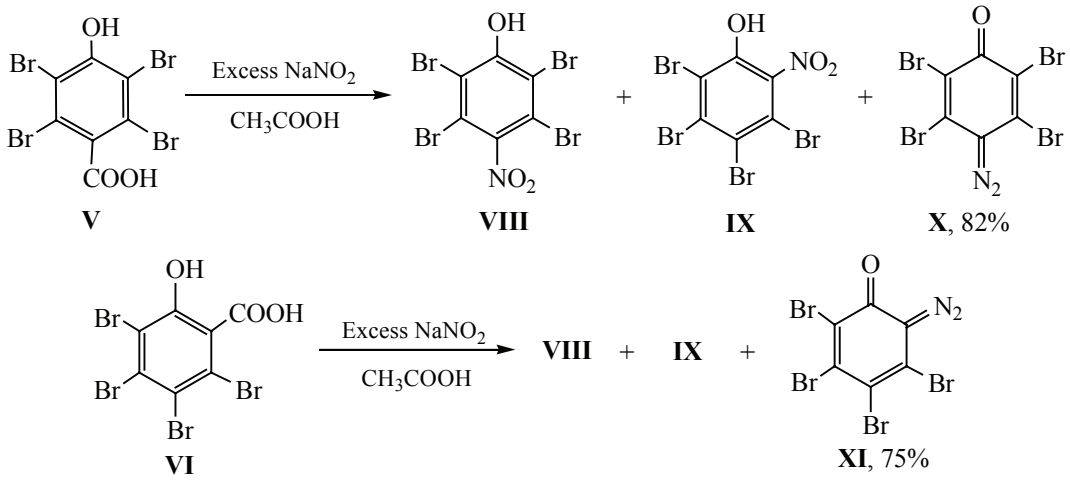
Tetrabromo-substituted acids **V, VI** were prepared by the bromination of dibromo-substituted acids **I, II** along modified procedures [2, 3]: acids **I, II** were treated with Br_2 not in the 60% oleum at 30°C, but in the 40% oleum at 35–40°C. This resulted in a considerable acceleration of the bromodesulfonation of the intermediately formed arenesulfonic acids, and the yield of the target products increased. The bromination of acid **Ia** with Br_2 in 30% oleum at 40−45°C provided tribromo-substituted acid

† Deceased.

VII in a 35% yield.

Tetrabromohydroxybenzoic acids **V, VI** compared with dibromo-substituted analogs **I, II** proved to be more active in the nitrosation reactions. For instance, the reaction of acid **V** with the 10-fold molar excess of $NaNO_2$ in the glacial acetic acid at 20°C was completed in 3 h. It resulted in a mixture containing products of the oxidative nitrosodecarboxylation: nitrophenols **VIII, IX**, and also tetrabromo-*p*-quinone diazide (**X**) in the molar ratio 2 : 1 : 37 (the data of the material balance of the reaction). The same nitrophenols **VIII, IX** in a mixture with tetrabromo-*o*-quinone diazide (**XI**) in the molar ratio 1 : 3 : 13 formed under these conditions from isomer **VI**.

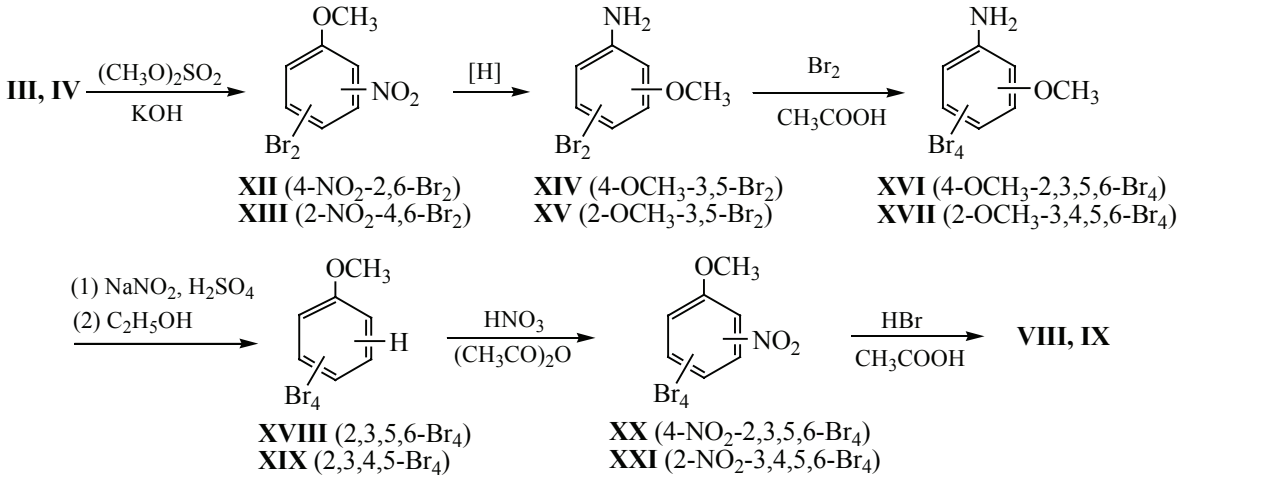
The main reaction products, crystalline quinone diazides **X, XI**, were separated by filteration after alkalinizing the reaction mixtures with 10% solution of Na_2CO_3. Isomeric nitrophenols **VIII, IX** were extracted with ethyl ether from the mother liquors acidified with dilute aqueous HCl till pH 1–2; these reaction products were identified as mixtures by the data of IR and ^{13}C NMR spectra. The estimation of the relative content of nitrophenols **VIII, IX** was performed using reference signals of methoxy groups in the ^1H NMR spectra of the corresponding anisols obtained in a quantitative yield by treating the mixtures of **VIII, IX** with dimethyl sulfate in alkaline medium.



The structure of compounds **X, XI** was proved by their spectral characteristics. In particular, in the IR spectra the diazo group gives rise to a characteristic absorption band at 2130 and 2136 cm^{-1} respectively, and the carbonyl group, to the band of stretching vibrations at ~1681 cm^{-1}. In the ^{13}C NMR spectra the signals of the carbonyl carbon atoms supporting the quinoid structure appear at 168.8 and 169.7 ppm respectively. The MALDI spectra correspond to the empirical formula.

The more reliable identification of compounds **VIII, IX** was obtained by the independent syntheses. To this end we first attempted to reproduce the sequence of procedures described in [4], however at the stage of tetrabromohydroxybenzoic acids **V, VI** decarboxylation by heating in *N*,*N*-dimethylaniline at 200°C intractable mixtures of products were obtained, and we failed to isolate therefrom the target products. Therefore taking into account the existing published data we developed a six-stage scheme of the synthesis of phenols **VIII, IX**.

We used as initial compounds nitrophenols **III, IV**. Their methylation with dimethyl sulfate in alkaline medium provided dibromonitroanisoles **XII, XIII**. Next stage of the nitro group reduction in compounds **XII**, **XIII** aroused some troubles. We found that nitroanisole **XII** could be reduced into anisidine **XIV** with the granulated tin in concn. HCl. Similar approach to the synthesis of anisidine **XV** was unsuccessful because of the low yield and difficulties in the isolation of this oily product. Therefore tetrabromoanisidine **XVII** was obtained in 67% yield by the reduction of dibromonitroanisole **XIII** with tin(II) chloride in a mixture of CH_3COOH and concn. HCl followed by the bromination of reaction product **XV** without its isolation from the reaction mixture. The stages of compound **XIV** bromination and anisidines **XVI, XVII** deamination occurred without complications. As a result the known tetrabromoanisoles **XVIII, XIX** were obtained [4] whose nitration with fuming nitric acid (d 1.52 g cm^{-1}) in acetic anhydride furnished nitroanisoles **XX, XXI**. The

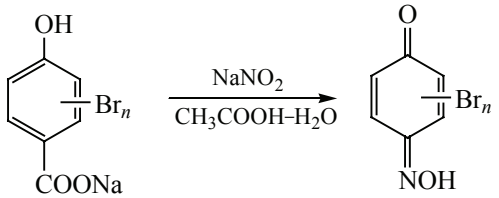


demethylation of nitroanisoles **XX, XXI** with a mixture of glacial CH_3COOH and concn. HBr (1 : 1) afforded individual nitrophenols **VIII, IX** in 61–70% yield[1] whose constants were in agreement with the published data [4].

We also established that the reaction of a water solution of acid **VI** sodium salt and a five-fold excess of $NaNO_2$ in glacial acetic acid at 20°C resulted in the formation only of quinone diazide **XI** in 50% yield. In the same conditions the sodium tetrabromohydroxybenzoate (**V**) quantitatively converted into quinone monooxime **XXII**.

Similarly from sodium salts of 3-bromo-4-hydroxybenzoic (**XXIII**) [5], dibromohydroxybenzoic (**Ia**), and tribromohydroxybenzoic (**VII**) acids the corresponding quinone monooximes **XXIV–XXVI** were obtained in high yields. Compound **XXIII** does not react with sodium nitrite in the glacial acetic acid, and its isomer, 5-bromo-2-hydroxybenzoic acid (**XXVII**) [6], same as acid **II**, does not react with $NaNO_2$ either in glacial or dilute acetic acid.

The structure of quinone monooximes **XXII, XXIV–XXVI** was confirmed by spectral data. For instance, the



Ia, V, VII, XXIII **XXII, XXIV–XXVI**

n = 1–4.

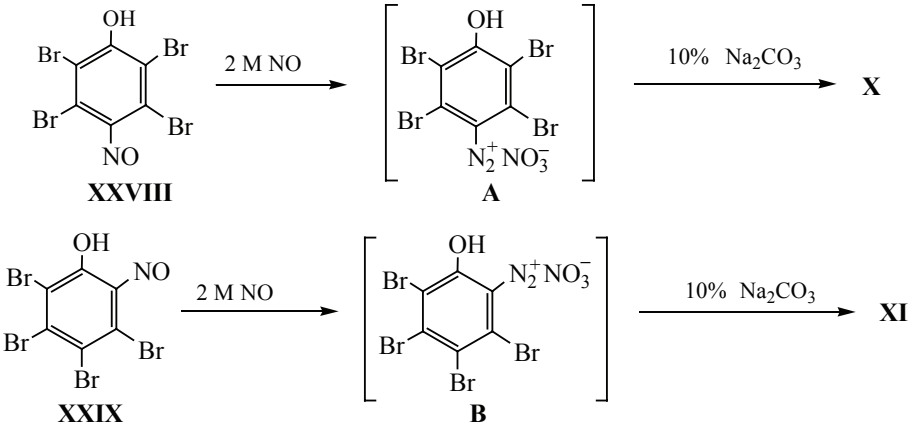
quinoid structure is supported by the presence in the IR spectra of strong bands in the region 1635–1643 cm^{-1}, and in the ^{13}C NMR spectra, of signals at 168–173 ppm belonging to the carbon atom of the conjugated carbonyl group.

In interpreting the results obtained we proceed from the electrophilic mechanism of the *ipso*-substitution in the nitrosodecarboxylation of polybrominated hydroxybenzoic acids involving the nitrosonium acetate generated in the reaction of $NaNO_2$ with CH_3COOH [7], which leads to the formation of the corresponding brominated nitrosophenol. We believe that the higher reactivity of tetrabromohydroxybenzoic acids **V, VI** compared with their dibromo-substituted analogs **I, II** is due to the *ortho*-effect of bromine atoms. The carboxy group in these compounds because of the steric repulsion is partially displaced from the conjugation with the aromatic ring and therefore does not deactivate the ring by the mesomeric effect to the electrophilic attack.

In event of tetrabromohydroxybenzoic acids **V, VI** the formation of the diazo compound from the nitrosophenol proves to be a prevailing process and parallel to it occurs a side reaction of nitrosophenol oxidation into nitrophenol. We presume that the reason of these processes consists in the fact that compared with the corresponding dibromo analogs the tetrabromo-substituted nitroso compounds **XXVIII, XXIX** because of the acceptor effect of the large number of halogen atoms in the ring possess a higher oxidative potential and are converted into nitrophenols only partially. The examples of diazo compounds formation in the nitrosodecarboxylation of hydroxybenzoic acids were already described earlier [8–10]. In [11] a mechanism was suggested of the transition of a nitroso compound into a diazonium nitrate under the action of

[1] In [4] nitroanisoles **XX, XXI** were demethylated using BBr_3 in benzene; the yields of nitrophenols **VIII, IX** were 1.5 and 31% respectively.

nitrogen oxides. In this connection it is reasonable to assume that nitrosophenols **XXVIII, XXIX** react with nitrogen oxides, e.g., with NO, and are transformed first into nitrates of diazophenols **A** and **B** respectively, and further at the treatment of the reaction mixtures with Na_2CO_3 solution give quinone diazides **X, XI**.



A qualitative confirmation of the formatation of diazophenol salts **A** and **B** at the nitrosodecarboxylation of acids **V, VI** is the reaction of azocoupling proceeding at the addition to the reaction mixture of the alkaline solution of β-naphthol resulting in the appearance of a dark red precipitate.

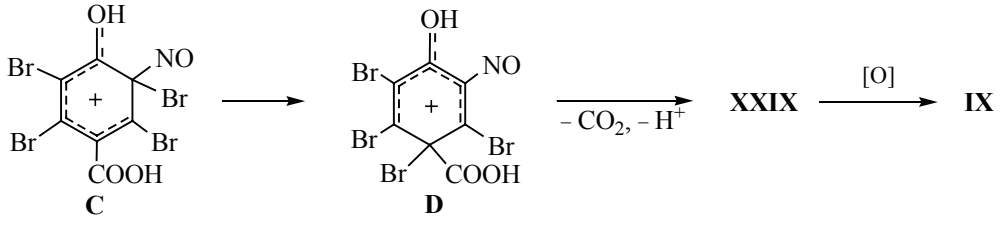
The formation of nitrophenol **IX** from acid **V** and of nitrophenol **VIII** from acid **VI** in reaction carried out in the glacial CH_3COOH indicates the occurrence of rearrangements in the *ipso*-nitroso complexes like at the oxidative nitrosodecarboxylation of acid **Ia** and salt **II**.

Thus in keeping with the orientation effect of the electron-donor hydroxy group the *ipso*-attack of the nitrosonium cation on acid **V** occurs with respect to this group both in the *para*- and *ortho*-positions giving an *ipso*-nitroso complex **C**. The rearrangement of this complex into *ipso*-bromo complex **D** and the decarboxylation of the latter results in nitrosophenol **XXIX** that further oxidates into nitrophenol **IX**.

It is possible analogously to rationalize the formation of compound **VIII** at the nitrosodecarboxylation of tetrabromosalicilic acid (**VI**).

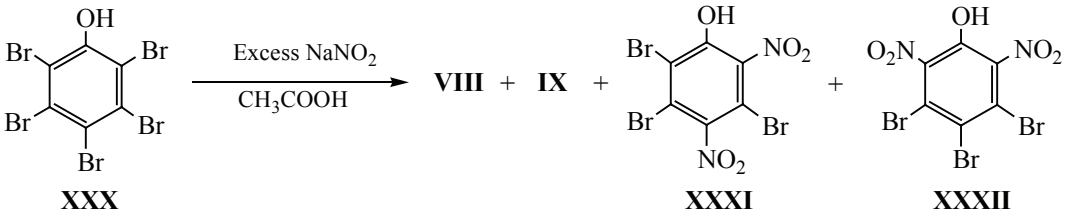
The rearrangements of the intermediate *ipso*-nitroso complexes occur apparently through intramolecular successive 1,2-shifts of bromine atoms via "bromonium" transition states [12]. But the intermolecular exchange of the *ipso*-nitroso complexes with the initial tetrabromohydroxybenzoic acids cannot be ruled out. A published analog of such process is the Reverdin rearrangement [13, 14] observed at the nitration of *p*-bromoanisole.

One possible product among those generated by the intermolecular rearrangement during the nitrosation of tetrabromohydroxybenzoic acids **V, VI** might be pentabromophenol **XXX**, cf. [14]. We did not detect even trace amounts of this compound among the products of nitrosodecarboxylation. At the same time it was established that the nitrosodebromination of phenol **XXX** occurred under



identical conditions slower than the nitrosodecarboxylation of compounds **V, VI**. The relatively high conversion (83%) was observed only after 5.5 h. The reaction products of compound **XXX** were the same nitrophenols **VIII, IX** in the ratio 1.4 : 1 with a small impurity consisting of two highly polar and well soluble compounds, presum-

ably, dinitrophenols **XXXI, XXXII**. The main reaction product, nitrophenol **VIII**, was isolated in an individual state in 22% yield.



XXX **XXXI** **XXXII**

but their conversion into the final products proceeds involving a stronger oxidant than HNO_2 and nitrogen oxides, namely, with a bromine cation liberated at the electrophilic *ipso*-substitution.

The lack of the pentabromophenol in the reaction mixtures during nitrosodecarboxylation of tetrabromo-substituted hydroxybenzoic acids suggests that the rearrangement of the *ipso*-nitroso complexes most likely occurs by the intramolecular mechanism.

The results of the nitrosation of compounds **I, V, VII, XXIII** in dilute acetic acid may be ascribed to the low solubility in the reaction mixture of the formed at the *ipso*-nitrosodecarboxylation brominated *p*-nitrosophenols which undergo a fast rearrangement into the corresponding more stable quinone monooximes **XXII, XXIV–XXVI** that precipitate. Quinone monooximes unlike nitrosophenols do not react with nitrogen oxides and nitrous acid [15].

Thus the nitrosation of tetrabromohydroxybenzoic **V, VI** and the other brominated hydroxybenzoic acids in CH_3COOH is a convenient method of the preparation of previously unknown quinone diazides **X, XI** and *p*-quinone monooximes **XXII, XXIV–XXVI**.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were registered on a spectrometer JNM-ECX400 JEOL (400.1 and 100.6 MHz respectively) from solutions of compounds in DMSO-d_6 and in some cases, in $CDCl_3$. The signals of residual protons and of carbon atoms of deuterated solvents served as reference signals for measuring the chemical shifts. A special feature of ^1H NMR spectra of some polybrominated phenols and anisidines in DMSO-d_6 is the absence of proton signals from hydroxy and amino groups. IR spectra were recorded on a Fourier spectrometer InfraLUM FT-02 from pellets with KBr. In the IR spectra 10 characteristic and the strongest absorption bands are reported.

The intermediate compounds in the nitrosodebromination of phenol **XXX** like in the nitrosodecarboxylation of acids **V, VI** are the same nitrosophenols **XXVIII, XXIX**

The conditions of analytical TLC are as follows: adsorbent Silufol UV-254, eluent hexane–acetone, 7 : 3, development in iodine chamber or under UV irradiation. The flash-chromatography was carried out using silica gel Merk L 5/40 μ, eluent light petroleum ether–acetone, 2–9 : 1. Elemental analyses were performed on a CHN-analyzer VarioMICRO.

Mass spectra MALDI were taken on an instrument Autoflex II Bruker (resolution FWHM 18000) equipped with a nitrogen laser with the operating wavelength 337 nm and a time-of-flight analyzer operating in a reflectron mode. Accelerating voltage 20 kV. The samples were deposited on a sublayer of polished steel. The spectra were registered in the positive ions mode. The resulting spectrum was a sum of 300 spectra taken in various points of the sample. 2,5-Dihydroxybenzoic acid (Acros, 99%) and α-cyano-4-hydroxycinnamic acid (Acros, 99%) were used as matrices.

3-Bromo-4-hydroxybenzoic acid (XXIII) was obtained in 76% yield by procedure [5], mp 176°C (aqueous C_2H_5OH) (mp 175–178°C [5]). IR spectrum, ν, cm^{-1}: 3301 br.m, 3078 w, 1677 v.s, 1581 m, 1377 m, 1299 v.s, 1249 s, 767 m. ^1H NMR spectrum, δ, ppm: 6.98 d (1H, H^5, *J* 8.7 Hz), 7.76 d.d (1H, H^6, *J* 2.3, 8.7 Hz), 7.99 d (1H, H^2, *J* 2.3 Hz), H_{arom}; 11.04 br.s (2H, COOH, OH). ^{13}C NMR spectrum, δ, ppm: 109.1, 116.0, 123.0, 130.5, 134.3, 158.2, 166.1 (COOH).

5-Bromo-2-hydroxybenzoic acid (XXVII) was obtained in 70% yield by procedure [6], mp 167°C (aqueous C_2H_5OH) (mp 165–166°C [6]). IR spectrum, ν, cm^{-1}: 3248 w, 3063 m, 3034–2843 ser.br. bands, 1655 v.s, 1608 s, 1473 s, 1442 v.s, 1196 s, 825 s, 686 m, 628 m. ^1H NMR spectrum, δ, ppm: 6.89 d (1H, H^3, *J* 8.7 Hz), 7.58 d.d (1H, H^4, *J* 2.75, 8.7 Hz), 7.82 d (1H, H^6, *J* 2.75 Hz), H_{arom}; 12.03 br.s (2H, COOH, OH). ^{13}C NMR spectrum, δ, ppm: 109.8, 115.1, 119.6, 132.1, 137.9, 160.1, 170.5 (COOH).

3,5-Dibromo-4-hydroxybenzoic acid (Ia) was obtained by procedure [16] in 81% yield, mp 200°C (aqueous C_2H_5OH) (mp 202°C [16]). IR spectrum, ν, cm^{-1}: 3449 w, 3080 w, 2964–2519 ser.br.bands, 1693 v.s, 1587 w, 1562 w, 1421 w, 1304 s, 1277 s, 765 w, 744 w. ^1H NMR spectrum, δ, ppm: 7.98 s (2H, $H^{2,6}$, H_{arom}). ^{13}C NMR spectrum, δ, ppm: 111.3 (2C), 124.6 (1C), 133.4 (2C), 154.7 (1C), 164.9 (COOH).

3,5-Dibromo-2-hydroxybenzoic acid (II) was obtained by procedure [17] in 87% yield, mp 201°C (aqueous C_2H_5OH) (mp 204°C [17]). IR spectrum, ν, cm^{-1}: 3209 w, 3094 w, 3059 w, 3000–2515 ser.br. bands, 1662 v.s, 1597 w, 1427 s, 1300 s, 1226 v.s, 1180 s, 713 s. ^1H NMR spectrum, δ, ppm: 7.84 d (1H, H^4, *J* 2.29 Hz), 7.98 d (1H, H^6, *J* 2.29 Hz), H_{arom}; 10.53 br.s (2H, OH, COOH). ^{13}C, δ, ppm: 109.9, 111.7, 115.9, 131.7, 139.8, 157.1, 170.4 (COOH).

Tetrabromohydroxybenzoic acids (V, VI). General procedure. To a solution of 10 g (34 mmol) of hydroxybenzoic acid **Ia** or **II** in 40 ml of 40% oleum was added dropwise at vigorous stirring within 0.5 h 3.2 ml (9.92 g, 62 mmol) of Br_2 maintaining the temperature of the reaction mixture at 35–40°C. The mixture was stirred at this temperature for 4 h and was left overnight. Then it was slowly poured on ice. The separated precipitate was filtered off, washed with water, and crystallized from aqueous ethanol with activated carbon.

2,3,5,6-Tetrabromo-4-hydroxybenzoic acid (V). Yield 65%, mp 227–228°C (mp 224°C[2]). IR spectrum, ν, cm^{-1}: 3528−2752 ser.br.bands, 1740 v.s, 1693 v.s, 1547 m, 1358 v.s, 1334 v.s, 1273 s, 1219 s, 1176 C, 640 m. ^1H NMR spectrum, δ, ppm: 11.05 br.s (2H, COOH, OH). ^{13}C NMR spectrum, δ, ppm: 115.6 (2C), 120.7 (2C), 133.5 (1C), 153.5 (1C), 166.5 (COOH).

3,4,5,6-Tetrabromo-2-hydroxybenzoic acid (VI). Yield 70%, mp 235−236°C (mp 235−240°C [3]). IR spectrum, ν, cm^{-1}: 3410 m, 3165–2746 ser.br.bands, 1709 v.s, 1701 v.s, 1558 s, 1358 m, 1273 s, 1203 m, 933 m, 671 m. ^1H NMR spectrum, δ, ppm: 8.67 br.s (2H, COOH, OH). ^{13}C NMR spectrum, δ, ppm: 116.5, 118.5, 120.5, 128.6, 129.1, 151.1, 165.8 (COOH).

2,3,6-Tribromo-4-hydroxybenzoic acid (VII). To a mixture of 10 g (34 mmol) of acid **Ia** and 80 ml of 30% oleum at vigorous stirring was added dropwise within 0.5 h 3.2 ml (9.92 g, 62 mmol) of Br_2 maintaining the temperature of the water bath at 40−45°C. The stirring at this temperature was continued for 4 h more, and the reaction mixture was left overnight at 20°C. Then it was slowly poured on ice. The separated precipitate was filtered off, washed with water, and dried in air. The reaction product was crystallized from aqueous ethanol with activated carbon. Yield 4.46 g (35%), mp 224–225°C. IR spectrum, ν, cm^{-1}: 3464 m, 3078 w, 3036–2862 ser.br. bands, 1709 v.s, 1566 m, 1358 s, 1296 s, 1192 s, 1095 m, 671 w. ^1H NMR spectrum, δ, ppm: 7.91 s (1H, H^5_{arom}). ^{13}C NMR spectrum, δ, ppm: 110.1, 117.5, 123.1, 128.2, 132.9, 154.3, 165.8 (COOH). Found, %: C 22.33; H 0.87. $C_7H_3Br_3O_3$. Calculated, %: C 22.43; H 0.81.

2,6-Dibromo-4-nitrophenol (III) was obtained by procedure [18] in 92% yield, mp 143°C (aqueous C_2H_5OH) (mp 144–145°C [18]). IR spectrum, ν, cm^{-1}: 3365 m, 3079 w, 1573 m, 1512 v.s, 1463 s, 1323 v.s, 1230 s, 1128 s, 898 m, 742 s. ^1H NMR spectrum, δ, ppm: 8.35 s (2H, $H_a^{3,5}{}_{r}{}_{om}$). ^{13}C NMR spectrum, δ, ppm: 111.0 (2C), 127.9 (2C), 140.0 (1C), 157.4 (1C).

4,6-Dibromo-2-nitrophenol (IV) was obtained by procedure [19] in 90% yield, mp 112–113°C (aqueous C_2H_5OH) (mp 115°C [19]). IR spectrum, ν, cm^{-1}: 3434 w, 3072 w, 1600 m, 1531 s, 1450 w, 1392 m, 1328 m, 1242 s, 1112 m. ^1H NMR spectrum, δ, ppm: 8.06 d (1H, H^5, *J* 2.29 Hz), 8.09 d (1H, H^3, *J* 2.29 Hz), H_{arom} ^{13}C NMR spectrum, δ, ppm: 108.3, 116.3, 126.9, 138.1, 139.8, 149.9.

Methylation of dibromonitrophenols III, IV. General procedure. At 20°C equimolar amounts were mixed of saturated ethanol solutions of nitrophenols **III** or **IV** and KOH. The separated precipitate was filtered off and dried in air. To boiling solution of 3 g (9 mmol) of the obtained potassium salts in 30 ml of dry acetone was added at stirring dropwise within 15 min 3 ml (4 g, 32 mmol) of dimethyl sulfate. The mixture was boiled for 1 h more, then it was cooled to room temperature and diluted with 70 ml of water. The separated precipitate was filtered off and heated for 10 min with 50 ml of 10% solution of KOH at 40–50°C. Insoluble in KOH the target reaction product was filtered off, washed with water, and crystallized from aqueous ethanol.

2,6-Dibromo-4-nitroanisole (XII). Yield 84%, mp 121°C (mp 123°C [20]). IR spectrum, ν, cm^{-1}: 3082 w, 2955 v.w, 1516 s, 1458 m, 1412 m, 1346 v.s, 1265 m, 1130 m, 972 s, 748 m. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.96 s (3H, OCH_3), 8.40 s (2H, $H_a^{3,5}{}_{r}{}_{om}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 61.0 (OCH_3), 118.5 (2C), 128.1 (2C), 144.2 (1C), 159.7 (1C).

4,6-Dibromo-2-nitroanisole (XIII). Yield 77%, mp 82°C (mp 80°C [21]). IR spectrum, ν, cm^{-1}: 3078

w, 2951 v.w, 1585 m, 1527 v.s, 1466 s, 1415 s, 1346 s, 1253 m, 976 s, 871 m. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.99 s (3H, OCH_3), 7.88 d (2H, H^5, *J* 2.29 Hz), 7.92 d (2H, H^3, *J* 2.29 Hz), H_{arom} ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 62.8 (OCH_3), 116.7, 120.8, 127.2, 140.0, 145.4, 150.1.

3,5-Dibromo-4-methoxyaniline (XIV). A mixture of 10 g (32 mmol) of nitroanisole **XII**, 11.5 g (97 mmol) of granulated tin, and 75 ml of concn. HCl was maintained for 1 h at 20°C, then the reaction mixture was heated on a water bath at 70–80°C over 5 h with intermittent stirring. The formed salt was filtered off, washed on the filter with a little ice water and afterwards it was treated with 2 M solution of $NaHCO_3$ till pH 6−7, and filtered. The obtained precipitate was dispersed in 150 ml of acetone. The mixture was filtered through a folded filter, the solvent was evaporated in a vacuum, the residue was crystallized from aqueous ethanol. Yield 6 g (67%), mp 69°C (mp 66°C [22]). IR spectrum, ν, cm^{-1}: 3414 w, 3337 m, 3078 v.w, 2928 w, 1597 s, 1550 m, 1516 m, 1473 v.s, 1230 s, 987 s, 744 s. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.62 br.s (2H, NH_2), 3.78 s (3H, OCH_3), 6.79 s (2H, $H_a^{3,}{}_r^{5}{}_{om}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 60.1 (OCH_3), 118.1 (2C), 118.5 (2C), 144.3 (1C), 146.0 (1C).

3,4,5,6-Tetrabromo-2-methoxyaniline (XVII). To a solution of 11.2 g (36 mmol) of dibromonitroanisole **XIII** and 170 ml of glacial acetic acid was added in succession 53 g (280 mmol) of $SnCl_2$ and 45 ml of concn. HCl. The reaction mixture was heated for 6 h on a water bath at 70–80°C. Then to it was added dropwise 4.1 ml (12.67 g, 79.2 mmol) of Br_2 in 30 ml of glacial acetic acid, and the mixture was stirred for 1.5 h at 50°C, cooled to room temperature and poured in water. The separated precipitate was filtered off, dried in air, and crystallized from light petroleum ether (bp 40–70°C). Yield 7.9 g (50%), mp 110°C (mp 112°C [22]). IR spectrum, ν, cm^{-1}: 3483 w, 3422 s, 2978 w, 1612 v.s, 1593 v.s, 1446 v.s, 1408 v.s, 1381 v.s, 1098 w, 999 v.s. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.81 s (3H, OCH_3), 4.56 br.s (2H, NH_2). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 59.5 (OCH_3), 111.0, 114.5, 120.1, 123.7, 140.0, 143.7.

2,3,5,6-Tetrabromo-4-methoxyaniline (XVI) was obtained by bromination of anisidine **XIV** by procedure [23] in 70% yield, mp 143°C (mp 145–146°C[23]). IR spectrum, ν, cm^{-1}: 3414 w, 3310 m, 2939 w, 1670 m, 1446 s, 1404 v.s, 1307 m, 1014 s, 821 m, 640 m. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.80 s (3H, OCH_3), 4.78 br.s (2H, NH_2). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 60.7 (OCH_3), 110.1 (2C), 120.9 (2C), 141.4 (1C), 146.9 (1C).

2,3,5,6-Tetrabromoanisole (XVIII) was obtained by diazotization of anisidine **XVI** with a subsequent reduction of the diazonium salt by procedure [23] in 50% yield, mp 119°C (mp 117–118°C [23]). IR spectrum, ν, cm^{-1}: 3082 w, 2978 w, 1585 w, 1531 s, 1388 s 1354 v.s, 1280 w, 1030 m, 1010 s, 945 m. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.87 s (3H, OCH_3), 7.72 s (1H, $H^4{}_{arom}$). ^{13}C ($CDCl_3$), δ, ppm: 60.5 (OCH_3), 120.9 (2C), 124.9 (2C), 132.6 (1C), 156.6 (1C).

2,3,4,5-Tetrabromoanisole (XIX) was obtained by diazotization of anisidine **XVII** with a subsequent reduction of the diazonium salt by procedure [23] in 45% yield, mp 141°C (mp 139–140°C [23]). IR spectrum, ν, cm^{-1}: 2924 w, 1558 s, 1450 w, 1404 s, 1331 s, 1269 s, 1068 w, 1057 w, 1022 w, 844 w. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.88 s (3H, OCH_3), 7.14 s (1H, $H^4{}_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 57.0 (OCH_3), 115.2, 115.4, 119.3, 124.4, 129.6, 156.2.

Nitration of tetrabromoanisoles XVIII, XIX. General procedure. To a solution of 1 g (2.35 mmol) tetrabromoanisole **XVIII** or **XIX** in 50 ml of acetic anhydride was poured in one portion 20 ml of fuming nitric acid (*d* 1.52 g/cm^3). After 1.5 min the reaction mixture was poured on ice. The separated precipitate was filtered off, washed with water, and crystallized from aqueous ethanol.

2,3,5,6-Tetrabromo-4-nitroanisole (XX). Yield 42%, mp 155°C (mp 159°C [4]). IR spectrum, ν, cm^{-1}: 2939 v.w, 1542 v.s, 1446 w, 1346 s, 1002 m, 744 v.w, 659 w, 621 w. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.92 s (3H, OCH_3). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 60.9 (OCH_3), 116.9 (2C), 122.8 (2C), 149.8 (1C), 157.2 (1C). Found, %: C 17.85; H 0.70; N 2.90. $C_7H_3Br_4NO_3$. Calculated, %: C 17.94; H 0.65; N 2.99.

3,4,5,6-Tetrabromo-2-nitroanisole (XXI). Yield 50%, mp 110°C (mp 116°C [4]). IR spectrum, ν, cm^{-1}: 2924 w, 1541 m, 1394 w, 1346 v.s, 1275 s, 1192 s. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.94 s (3H, OCH_3). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 63.3 (OCH_3), 115.9, 122.6, 125.5, 131.9, 147.1, 149.2. Found, %: C 17.80; H 0.63; N 3.05. $C_7H_3Br_4NO_3$. Calculated, %: C 17.94; H 0.65; N 2.99.

Demethylation of tetrabromonitroanisoles XX, XXI. General procedure. A mixture of 1 g (2.1 mmol) of nitroanisole **XX** or **XXI**, 15 ml of glacial CH_3COOH, and 15 ml of concn. HBr was boiled for 6 h and left overnight at room temperature. Afterwards the reaction mixture was diluted with water to 130 ml. The separated precipitate

was filtered off, washed with water, and heated with 50 ml of 10% KOH solution for 10 min. The insoluble solid was unreacted anisole **XX** or **XXI** that was filtered off. The mother liquor was acidified with concn. HCl till pH 1–2. The reaction product was filtered off and purified by crystallization from aqueous ethanol.

2,3,5,6-Tetrabromo-4-nitrophenol (VIII). Yield 70%, mp 186°C (decomp.) {mp 187°C (decomp.) [4]}. IR spectrum, ν, cm^{-1}: 3404 m, 1542 v.s, 1446 w, 1346 C, 1002 m, 744 v.w, 659 w, 621 w. ^{13}C NMR spectrum, δ, ppm: 115.9 (2C), 116.3 (2C), 145.4 (2C), 155.1 (2C). Found, %: C 15.97; H 0.17; N 2.96. $C_6HBr_4NO_3$. Calculated, %: C 15.85; H 0.22; N 3.08.

2,3,5,6-Tetrabromo-2-nitrophenol (IX). Yield 61%, mp 196°C (mp 195°C [4]). IR spectrum, ν, cm^{-1}: 3472 m, 1535 v.s, 1369 m, 1412 m, 1269 m, 941 w, 891 w. ^{13}C NMR spectrum, δ, ppm: 115.2, 118.1, 118.3, 130.7, 142.6, 147.1. Found, %: C 15.78; H 0.26; N 3.06. $C_6HBr_4NO_3$. Calculated, %: C 15.85; H 0.22; N 3.08.

Reactions of tetrabromohydroxybenzoic acids V, VI with $NaNO_2$ in glacial acetic acid. General procedure. To a solution of 1.59 g (3.5 mmol) of hydroxybenzoic acid **V** or **VI** in 50 ml of glacial CH_3COOH while stirring at 20°C was added by small portions 2.42 g (35 mmol) of $NaNO_2$ within 2 h. The reaction mixture was stirred for 1 h more and poured into 200 ml of 10% solution of Na_2CO_3. The separated precipitate was filtered off and dissolved in 30 ml of CH_2Cl_2. The organic solution was washed with a saturated solution of $NaHCO_3$ (3 × 10 ml), with water, and dried with Na_2SO_4. On removing the solvent in a vacuum of the water-jet pump we obtained 0.89 g of light-yellow crystals of compound **X** or 0.73 g of red-brown crystals of compound **XI**. The mother liquor was acidified with concn. HCl till pH 1–2 and was diluted with water till 500 ml, then it was extracted with ethyl ether (5 × 50 ml.) The combined ether extracts were washed with water, dried with Na_2SO_4, the solvent was evaporated. We obtained 0.08 g of a mixture of tetrabromonitrophenols **VIII, IX** in a ratio 2:1 from acid **V** and 0.20 g of the mixture in a ratio 1:3 from acid **VI**. Compounds **VIII, IX**were identified by methods of TLC, IR and ^{13}C NMR spectroscopy; their relative content in the mixtures was determined by ^1H NMR spectroscopy after the quantitative conversion into the corresponding nitroanisoles **XX, XXI** by the procedure described above for compounds **XII, XIII**.

2,3,5,6-Tetrabromo-*p*-quinone diazide (X). Yield 82%, mp 132–133°C (decomp.). IR spectrum, ν, cm^{-1}: 2130 v.s, 1682 m, 1604 v.s, 1535 s, 1388 m, 1280 s, 1099 s, 744 m, 636 m. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 122.1 (2C), 123.0 (2C), 138.3 (1C), 168.8 (1C). MALDI spectrum: *m*/*z* 431.0315 $[M]^+$. $C_6Br_4N_2O$. Calculated *M* 431.7511.

3,4,5,6-Tetrabromo-*o*-quinone diazide (XI). Yield 75%, mp 137–138°C (decomp.). IR spectrum, ν, cm^{-1}: 2136 m, 1681 s, 1612 m, 1542 s, 1427 m, 1215 m, 1053 s, 702 w, 644 w. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 111.4, 113.4, 126.3, 138.4, 140.5, 169.7. MALDI spectrum: *m*/*z* 432.3546 $[M + H]^+$. $C_6Br_4N_2O$. Calculated *M* 432.7511.

Reaction of hydroxybenzoic acids I, V–VII, XXIII with $NaNO_2$ in dilute acetic acid. General procedure. Hydroxybenzoic acid **I, V–VII, XXIII** was dissolved in a minimum volume of ethanol and mixed with equimolar amount of NaOH also dissolved in a minimum volume of ethanol. The solvent was distilled off in a vacuum of the water-jet pump. The salt obtained in a quantitative yield was dried in air and was stored in a tightly stoppered weighing glass. In 70 ml of water was dissolved at stirring 3 mmol of the sodium salt of hydroxybenzoic acid **I, V–VII, XXIII** and 15 mmol of $NaNO_2$. Then at 20°C was added dropwise within 1 h 10 ml of glacial CH_3COOH, and the mixture was stirred for 3 h. The separated precipitate was filtered off, washed on the filter with water till neutral washings. From acid **VI** by treating the precipitate along the above procedure quinone diazide **XI** was obtained in 50% yield. In the other cases the precipitate consisted of the corresponding *p*-quinone monooxime **XXII, XXIV–XXVI** which after drying in air was purified by crystallization from aqueous ethanol.

2,3,5,6-Tetrabromo-*p*-quinone monooxime (XXII). Yield 95%, mp 115–116°C (decomp.). IR spectrum, ν, cm^{-1}: 3480 m, 1643 v.s, 1500 s, 1415 s, 1130 s, 868 m, 652 m. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 124.5 (2C), 128.5 (2C), 151.8 (1C), 168.2 (C=O). MALDI spectrum: *m*/*z* 435.2561 $[M + H]^+$. $C_6HBr_4NO_2$. Calculated *M* 435.7517.

2-Bromo-*p*-quinone monooxime (XXIV). Yield 55%, mp 140–141°C (decomp.). IR spectrum, ν, cm^{-1}: 3198 m, 3071 w, 1635 v.s, 1620 v.s, 1419 m, 1261 m, 1207 m, 1026 s, 871 m. ^1H NMR spectrum, δ, ppm: 6.63 d (1H, H^5, *J* 8.5 Hz), 7.54 d.d (1H, H^6, *J* 2.3, 8.5 Hz), 8.11 d (1H, H^2, *J* 2.3 Hz). ^{13}C NMR spectrum, δ, ppm: 124.1, 128.0, 138.4, 145.5, 149.2, 168.3 (C=O). Found, %: C 35.50; H 2.22; N 6.81. $C_6H_4BrNO_2$. Calculated, %: C 35.67; H 2.00; N 6.93.

2,6-Dibromo-*p*-quinone monooxime (XXV). Yield 89%, mp 156–157°C (decomp.). IR spectrum, ν, cm^{-1}: 3186 m, 3074 m, 1635 v.s, 1543 m, 1419 m, 1261 v.s,

1057 m, 1014 m, 875 m, 717 m. ^{1}H NMR spectrum, δ, ppm: 8.05 s (2H, $H^{2,6}$). ^{13}C NMR spectrum, δ, ppm: 126.0 (2C), 133.4 (2C), 148.8 (1C), 173.1 (C=O). Found, %: C 25.50; H 1.20; N 4.81. $C_6H_3Br_2NO_2$. Calculated, %: C 25.65; H 1.08; N 4.99.

2,3,6-Tribromo-*p*-quinone monooxime (XXVI). Yield 93%, mp 120–121°C (decomp.). IR spectrum, ν, cm^{-1}: 3260 br.m, 3063 w, 1643 v.s, 1531 m, 1393 m, 1292 m, 1200 m, 1064 s, 906 m, 733 w. ^{1}H NMR spectrum, δ, ppm: 8.26 s (1H, H^5). ^{13}C NMR spectrum, δ, ppm: 126.3, 128.8, 134.7, 136.9, 147.1, 172.0 (C=O). MALDI spectrum: m/z 357.1143 $[M+H]^+$. $C_6H_2Br_3NO_2$. Calculated M 357.8413.

Pentabromophenol (XXX). *a*. To a mixture of 35 ml (12.6 g, 687 mmol) of dry Br_2 and 3 g (11.2 mmol) of anhydrous $AlBr_3$ was added dropwise within 16.28 g (58.1 mmol) of anisole with intermittent stirring. The reaction mixture was kept for 12 h more at 20°C, then the excess bromine was distilled off, the solid product was washed with 5% solution of Na_2SO_3 till complete decoloration, and it was extracted with hot 10% NaOH solution (6 × 50 ml). The hot solution was filtered through a folded filter, the filtrate was neutralized with concn. HCl to a weakly acidic reaction by an indicator paper. The separated precipitate was filtered off, washed with water on the filter, and dried in air. Yield 24.2 g (90%), mp 223–224°C (CH_3COOH) (mp 230°C [24]). IR spectrum, ν, cm^{-1}: 3414 C, 1516 m, 1346 v.s, 1277, 1196 m, 933 w, 682 w. ^{13}C NMR spectrum, δ, ppm: 115.6 (2C), 118.1 (1C), 127.4 (2C), 152.5 (1C). Found, %: C 14.62; H 0.42. C_6HBr_5O. Calculated, %: C 14.75; H 0.21.

b. Similarly phenetole was brominated. Yield 93%, mp 224–225°C (CH_3COOH).

Reaction of pentabromophenol (XXX) with $NaNO_2$ in glacial acetic acid. To a solution of 1 g (2 mmol) of pentabromophenol (**XXX**) in 150 ml of glacial CH_3COOH was added at stirring at 20°C with small portions within 5.5 h 1.38 g (20 mmol) of $NaNO_2$, and the stirring was continued for 0.5 h more. The reaction mixture was diluted with water to 500 ml. The separated precipitate was filtered off and dried in air. This precipitate (0.7 g) according to the ^{1}H NMR spectrum of anisoles obtained from it consisted of unreacted pentabromophenol (**XXX**) and nitrophenols in a molar ratio 0.6 : 1.4 : 1.0. By means of flash-chromatography 0.2 g (22%) of compound **VIII** was isolated in the individual state. The filtrate was extracted with ethyl ether (5 × 50 ml). The combined extracts were dried with Na_2SO_4 and evaporated. We obtained 0.18 g of solid residue that was subjected to column chromatography on silica gel to give ~50 mg of yellow crystals, presumably, a mixture of dinitrophenols **XXXI, XXXII**. ^{13}C NMR spectrum, δ, ppm: 105.3, 117.7, 119.1, 119.5, 139.8, 141.4, 145.6, 149.1, 153.6, 157.2. Found, %: C 16.95; H 0.11; N 6.48. $C_6HBr_3N_2O_5$. Calculated, %: C 17.13; H 0.24; N 6.66.

REFERENCES

1. Shishkin, V.N. and Fadin, M.V., *Zh. Org. Khim.,* 2008, vol. 44, p. 697.
2. Pfanz, H. and Dorn, H., *Arch. Pharm.*, 1956, vol. 289, p. 651.
3. Larkin, H.F., Stuart, A.P., and Twiss, D., *J. Org. Chem.*, 1940, vol. 62, p. 1237.
4. Harrison, C.R. and McOmie, J.F.W., *J. Chem. Soc. C*, 1966, p. 997.
5. Tee, O.S., Iyengar, N.R., and Kraus, B., *J. Org. Chem.,* 1985, vol. 50, p. 973.
6. Hussey, A.S. and Wilk, I.J., *J. Am. Chem. Soc.,* 1950, vol. 72, p. 830.
7. Belyaev, E.Yu. and Gidaspov, B.V., *Aromaticheskie nitrozosoedineniya* (Aromatic Nitrocompounds), St. Petersburg: Teza, 1996.
8. Tedder, J.M. and Theaker, G., *J. Chem. Soc*., 1959, p. 257.
9. Nemodruk, A.A., *Zh. Obshch. Khim.,* 1958, vol. 28, p. 1082.
10. Nemodruk, A.A., *Zh. Obshch. Khim.,* 1956, vol. 26, p. 3283.
11. Tedder, J.M., *Tetrahedron*, 1959, vol. 5, p. 288.
12. Jacquesy, J.-C. and Jouannetaud, M.-P., *Tetrahedron Lett*., 1982, vol. 23, p. 1673.
13. Reverdin, F., Ber., 1896, vol. 29, p. 2595.
14. Perrin, C.L. and Skinner, G.A., *J. Am. Chem. Soc.*, 1971, vol. 93, p. 3389.
15. Nesmeyanov, A.N. and Ioffe, S.T., *Zh. Obshch. Khim.,* 1941, vol. 11, p. 393.
16. Robertson, W., *J. Chem. Soc.*, 1902, vol. 81, p. 1482.
17. Earle, R.B. and Jackson, H.L., *J. Am. Chem. Soc.*, 1906, vol. 28, p. 111.
18. *Sint. Org. prep*., 1949, vol. 2, p. 185.
19. Guben, I., *Metody organicheskoi khimii* (Methods of Organic Chemistry), Leningrad: Goskhimizdat, 1949, vol. 4, no. 1, p. 317.
20. Yamagishi, H., Matsumoto, K., Iwasaki, K., Miyazaki, T., Yokoshima, S., Tokuyama, H., and Fukuyama, T.,*Synth. Commun*., 1984, vol. 10, p. 2369.
21. Kohn, M. and Krasso, O., *J. Org. Chem*., 1946, vol. 11, p. 641.
22. Robertson, W., *J. Chem. Soc., Perkin Trans*., 1902, vol. 81, p. 1475.
23. Shishkin, V.N., Tanaseichuk, B.S., Lapin, K.K., Ivkina, A.A., and Butin, K.P., *Zh. Org. Khim.*, 1984, vol. 20, p. 2588.
24. Garman, J.A., Mamuzic, R.I., McDonald, R.B., Sands, J.L., and Thompson, G., Swiss Patent 647491, 1985; *Ref. Zh. Khim*., 1985, 24N144P.