

## Cross Coupling of Polybromiodobenzenes with Some Terminal Alkynes

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**Abstract**—Sonogashira reactions of pentabromiodobenzene and tetrabromo-1,4-diodobenzene with various terminal alkynes at 20°C in benzene resulted in selective replacement of the iodine atoms with formation of the corresponding alk-1-yn-1-yl-substituted polybromobenzenes.

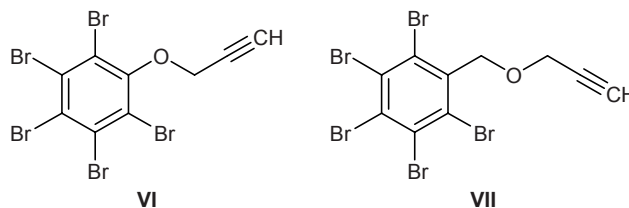
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We previously showed [1] that nucleophilic replacement of bromine in reactions of polybromoaromatics with nucleophiles is almost always accompanied by side reductive debromination with participation of solvent molecules as source of hydrogen. Moreover, in some cases, reductive debromination becomes the main reaction pathway. For example, the reaction of hexabromobenzene with sodium acetylide in liquid ammonia gives exclusively the corresponding reductive debromination product, 1,2,4,5-tetrabromobenzene [2]. Therefore, synthesis of functional derivatives of the polybromoaromatic series via direct nucleophilic replacement of bromine in polybromobenzenes by ethynyl groups seems to be improbable.

In the recent years, substitution of halogen in aryl halides via cross coupling reactions catalyzed by transition metal complexes has been extensively studied [3]. In most cases, such reactions with polybromoaromatic compounds lead to exhaustive replacement of all bromine atoms in the aromatic ring. Analogous reactions with polyiodoarenes occur much more readily and under milder conditions. It was noted that the reactivity of aryl iodides is higher by 5–6 orders of magnitude than the reactivity of the corresponding aryl bromides [4, 5]. Taking the above stated into account, we anticipated that cross coupling with aromatic compounds containing simultaneously bromine and iodine atoms should result in preferential or exclusive replacement of the iodine atoms.

In the present work we examined cross coupling of pentabromiodobenzene (**I**) and 1,2,4,5-tetrabromo-

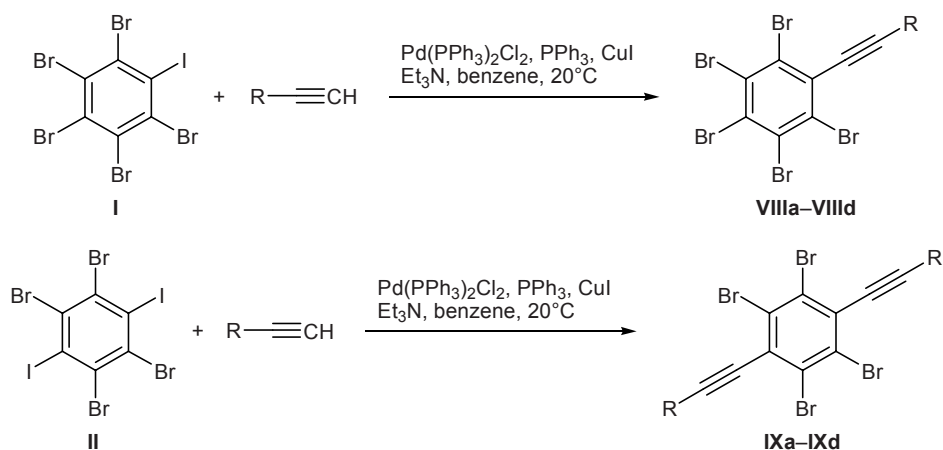
3,6-diodobenzene (**II**) with some terminal alkynes under the Sonogashira reaction conditions [6]. All reactions were carried out in benzene at 20°C under argon using bis(triphenylphosphine)palladium(II) chloride as catalyst, copper(I) iodide as co-catalyst, and triethylamine as base. The initial polybromiodobenzenes were synthesized by iodination of the corresponding polybromobenzenes in the system I<sub>2</sub>–KIO<sub>3</sub>–concd. H<sub>2</sub>SO<sub>4</sub> [7]. As terminal alkynes we selected prop-2-yn-1-ol (**III**), prop-2-yn-1-yl acetate (**IV**), phenylacetylene (**V**), and prop-2-yn-1-yl ethers **VI** and **VII** having a polybrominated benzene ring [2].



Compounds **I** and **II** failed to react with prop-2-yn-1-ol (**III**): after 24 h, only the initial polybromiodobenzenes were isolated from the reaction mixtures. No reaction occurred between these compounds on prolonged heating. However, in the presence of even traces of oxygen hexa-2,4-diyne-1,6-diol was always formed as a result of oxidative dimerization of prop-2-yn-1-ol. Prop-2-yn-1-yl acetate (**IV**) is less prone to undergo oxidative dimerization, and the reaction of **IV** with halogen derivatives **I** and **II** gave the corresponding cross-coupling products even in the presence of traces of oxygen in the reaction mixture. The reaction of **IV** with **I** in 24 h afforded acetate **VIIIa** in 23%

<sup>†</sup> Deceased.

Scheme 1.



yield (Scheme 1). The yield of **VIIIa** increased to 33% when the reaction time was prolonged to 48 h, but the yield was not improved upon further increase of the reaction time and the amount of catalyst. At 80°C the yield of **VIIIa** reached 44%, but the reaction was accompanied by replacement of bromine atoms, which complicated isolation of the target product from the reaction mixture. Thus raising the temperature reduces the selectivity of cross coupling. By analogous reaction of compound **II** with prop-2-yn-1-yl acetate (**IV**) (reaction time 48 h) we obtained 34% of diacetate **IXa** as a result of replacement of both iodine atoms (Scheme 1). Cross couplings of compounds **I** and **II** with alkynes **V–VII** were performed under the same conditions (only the reaction time was varied), and compounds **VIIIb–VIIId** and **IXb–IXd** were formed in satisfactory yields.

Thus the proposed conditions ensure selective cross coupling with replacement of only iodine atoms in polybromiodoaromatic compounds. The described approach demonstrates broad synthetic potential of polybromiodobenzenes. Introduction of ethynyl fragments into polybromoarene molecules makes them promising precursors of other classes of organic compounds containing a polybrominated benzene ring, which could be obtained by transformations involving the triple bond.

## EXPERIMENTAL

The IR spectra were recorded in KBr on an InfraLYuM FT-02 instrument. The <sup>1</sup>H NMR spectra were measured on a Bruker AC-200 spectrometer at an operating frequency of 200 MHz) from solutions in

DMSO-*d*<sub>6</sub> using hexamethyldisiloxane as internal reference. Thin-layer chromatography was performed on Silufol UV-254 plates using hexane–ethyl acetate (20:1) as eluent; spots were detected by treatment with iodine vapor or under UV light. The purity of the initial compounds and reaction products was checked by GLC on a Chrom-42 chromatograph equipped with a thermal ionization detector and a glass column, 3000×3.5 mm, packed with 3% of OV-17 on Chromaton N-Super (0.16–0.20 mm); oven temperature 220–260°C; carrier gas nitrogen. All individual compounds had a purity of no less than 97.5–98.5%.

Pentabromobenzene [8], prop-1-yn-1-yl acetate (**IV**) [9], 3-(2,3,4,5,6-pentabromophenoxy)prop-1-yne (**VI**) [2], and 3-(2,3,4,5,6-pentabromobenzyloxy)prop-1-yne (**VII**) [2] were synthesized according to known procedures.

**1,2,4,5-Tetrabromobenzene.** A solution of AlBr<sub>3</sub> in bromine [0.6 g (0.02 mol) of aluminum was burned in 45 ml (0.9 mol, 140 g) of bromine] was diluted with 200 ml of anhydrous carbon tetrachloride and added under stirring to 17 ml (0.2 mol, 14.9 g) of anhydrous benzene so that to avoid strong heating (the flask was cooled with an ice–water mixture). When the addition was complete (~ 1 h), the mixture was stirred for 30 min at 20°C and for 2 h at 50–60°C. Excess bromine was distilled off together with carbon tetrachloride, and the precipitate was filtered off, washed with a 10% solution of Na<sub>2</sub>SO<sub>3</sub> and water, dried in air, and recrystallized from toluene. Yield 33 g (44%), colorless crystals, mp 180–182°C; published data [10]: mp 181°C. IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3068 m, 1740 w, 1445 m, 1421 s, 1293 m, 1111 m, 1020 s, 880 s, 668 m, 521 m, 433 m. <sup>1</sup>H NMR spectrum:  $\delta$  7.87 ppm, s.

Found, %: C 18.36; H 0.49.  $C_6H_2Br_4$ . Calculated, %: C 18.31; H 0.51.

**Pentabromoiodobenzene (I).** A mixture of 2.5 g (0.01 mol) of  $KIO_3$ , 17.7 g (0.07 mol) of iodine, and 50 ml of concentrated sulfuric acid was stirred for 30 min, a suspension of 12 g (0.02 mol) of pentabromobenzene in 100 ml of concentrated sulfuric acid was added, and the mixture was stirred for 7 days at 18–20°C. It was then poured onto ice, a 10% solution of  $Na_2SO_3$  was added to remove excess iodine, and the precipitate was filtered off, dried over  $H_2SO_4$  with protection from light, and recrystallized from benzene. Yield 15 g (98%), colorless needles, mp 315–317°C; published data [11]: mp 318°C. IR spectrum,  $\nu$ ,  $cm^{-1}$ : 1284 s, 1249 m, 1242 m.

**1,2,4,5-Tetrabromo-3,6-diiodobenzene (II).** A mixture of 5.1 g (0.02 mol) of  $KIO_3$ , 42.6 g (0.17 mol) of iodine, and 60 ml of concentrated sulfuric acid was stirred for 30 min, a suspension of 12 g (0.03 mol) of 1,2,4,5-tetrabromobenzene in 72 ml of concentrated sulfuric acid was added, and the mixture was stirred for 5 days at 18–20°C. The mixture was then treated as described above in the synthesis of pentabromoiodobenzene (I) to isolate 12.7 g (82%) of compound II as colorless long needles with mp 328–330°C; published data [6]: mp 330°C. IR spectrum,  $\nu$ ,  $cm^{-1}$ : 1278 s, 1244 m, 1228 m.

**Reactions of polybromoiodobenzenes I and II with alkynes III–VII (general procedure).** A solution of 0.77 mmol of polybromoiodobenzene I or II in 80 ml of anhydrous benzene was purged with argon, 5 ml of triethylamine, 0.1 g (0.52 mmol) of  $CuI$ , and 0.77 mmol (in the reactions with I) or 1.54 mmol (in the reactions with II) of alkyne III–VII were added, the mixture was stirred for 10–15 min, 0.02 g (1 mol %) of  $Pd(PPh_3)_2Cl_2$  and 0.04 g (0.015 mmol) of  $PPh_3$  were added, and the mixture was purged again with argon, and stirred at 18–20°C until the reaction was complete. The solvent was removed under reduced pressure, the residue was dried in air, and the products were isolated by extraction into hexane or petroleum ether; in some cases, the products were additionally purified by flash chromatography on silica gel using hexane–ethyl acetate (20:1) as eluent.

**3-(2,3,4,5,6-Pentabromophenyl)prop-2-yn-1-yl acetate (VIIIa).** Reaction time 48 h; yield 33%, colorless crystals, mp 23–25°C (from petroleum ether). IR spectrum,  $\nu$ ,  $cm^{-1}$ : 2191 w, 1747 s, 1552 w, 1437 m, 1375 m, 1221 s, 1161 m, 1120 m, 1030 m, 866 w, 829 w, 750 w, 723 m, 696 m, 542 s.  $^1H$  NMR spec-

trum,  $\delta$ , ppm: 2.04 s (3H,  $CH_3$ ), 4.79 s (2H,  $CH_2$ ). Found, %: C 24.02; H 0.94.  $C_{11}H_5Br_5O_2$ . Calculated, %: C 23.23; H 0.89.

**1,2,3,4,5-Pentabromo-6-(phenylethynyl)benzene (VIIIb).** Reaction time 24 h; yield 53%, colorless crystals, mp 80–81°C (from hexane). IR spectrum,  $\nu$ ,  $cm^{-1}$ : 2147 w, 1550 m, 1522 m, 1483 m, 1367 m, 1294 m, 1159 m, 1024 w, 914 m, 854 m, 754 s, 721 w, 684 s, 540 w, 524 m.  $^1H$  NMR spectrum:  $\delta$  7.34–7.66 ppm, m ( $C_6H_5$ ). Found, %: C 30.12; H 0.76.  $C_{14}H_5Br_5$ . Calculated, %: C 29.36; H 0.88.

**1,2,3,4,5-Pentabromo-6-[3-(2,3,4,5,6-pentabromophenoxy)prop-2-yn-1-yl]benzene (VIIIc).** Reaction time 72 h; yield 48%, colorless crystals, mp 280–281°C (from petroleum ether). IR spectrum,  $\nu$ ,  $cm^{-1}$ : 2970 w, 2928 w, 2866 w, 2851 w, 1508 m, 1435 m, 1419 m, 1334 s, 1184 m, 1157 m, 1118 s, 1060 m, 999 s, 933 m, 721 m, 694 m, 682 m.  $^1H$  NMR spectrum:  $\delta$  4.98 ppm, s ( $CH_2$ ). Found, %: C 19.21; H 0.28.  $C_{15}H_2Br_{10}O$ . Calculated, %: C 18.07; H 0.20.

**1,2,3,4,5-Pentabromo-6-[3-(2,3,4,5,6-pentabromobenzyloxy)prop-2-yn-1-yl]benzene (VIIId).** Reaction time 96 h; yield 62%, colorless crystals, mp 293–295°C (from petroleum ether). IR spectrum,  $\nu$ ,  $cm^{-1}$ : 2939 w, 2878 w, 1508 m, 1435 m, 1323 m, 1188 m, 1118 m, 1080 s, 1057 m, 995 w, 748 w, 721 m, 694 m, 540 s.  $^1H$  NMR spectrum,  $\delta$ , ppm: 4.41 s (2H,  $CH_2$ ), 4.99 s (2H,  $CH_2$ ). Found, %: C 19.52; H 0.51.  $C_{16}H_4Br_{10}O$ . Calculated, %: C 19.00; H 0.40.

**3-[4-(3-Acetoxyprop-2-yn-1-yl)-2,3,5,6-tetrabromophenyl]prop-2-yn-1-yl acetate (IXa).** Reaction time 48 h; yield 34%, colorless crystals, mp 69–71°C (from petroleum ether). IR spectrum,  $\nu$ ,  $cm^{-1}$ : 2253 w, 1749 s, 1442 m, 1377 m, 1221 s, 1159 w, 1032 m, 1020 m, 879 m, 723 w, 696 w, 603 w, 542 m, 522 w.  $^1H$  NMR spectrum,  $\delta$ , ppm: 2.04 s (3H,  $CH_3$ ), 4.79 s (2H,  $CH_2$ ). Found, %: C 31.96; H 1.67.  $C_{16}H_{10}Br_4O_4$ . Calculated, %: C 32.80; H 1.72.

**1,2,4,5-Tetrabromo-3,6-bis(phenylethynyl)benzene (IXb).** Reaction time 24 h; yield 44%, colorless crystals, mp 152–154°C (from hexane). IR spectrum,  $\nu$ ,  $cm^{-1}$ : 2145 w, 1483 m, 1437 m, 1020 m, 914 m, 879 w, 848 w, 754 s, 723 w, 684 s, 524 m.  $^1H$  NMR spectrum:  $\delta$  7.56–7.61 ppm, m ( $C_6H_5$ ). Found, %: C 45.02; H 1.68.  $C_{22}H_{10}Br_4$ . Calculated, %: C 44.49; H 1.70.

**1,2,4,5-Tetrabromo-3,6-bis[3-(2,3,4,5,6-pentabromophenoxy)prop-1-yn-1-yl]benzene (IXc).** Reaction time 48 h; yield 72%, colorless crystals,

mp 280–281°C (from hexane). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2972 w, 2910 w, 2162 w, 1379 w, 1334 s, 1321 s, 1080 w, 1001 m, 978 m, 960 m, 914 w, 792 w, 733 w, 694 w, 669 w, 626 w, 557 w.  $^1\text{H}$  NMR spectrum:  $\delta$  4.98 ppm, s ( $\text{CH}_2$ ). Found, %: C 21.13; H 0.48.  $\text{C}_{24}\text{H}_4\text{Br}_{14}\text{O}_2$ . Calculated, %: C 20.58; H 0.55.

**1,2,4,5-Tetrabromo-3,6-bis[3-(2,3,4,5,6-pentabromobenzyloxy)prop-1-yn-1-yl]benzene (IXd).** Reaction time 48 h; yield 80%, colorless crystals, mp 173–175°C (from hexane). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2943 w, 2889 w, 2125 w, 1514 m, 1419 m, 1323 s, 1186 m, 1084 s, 1060 m, 1020 m, 993 w, 879 m, 721 w, 669 m, 607 w, 542 m.  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 4.40 s (2H,  $\text{CH}_2$ ), 4.99 s (2H,  $\text{CH}_2$ ). Found, %: C 21.52; H 0.46.  $\text{C}_{26}\text{H}_8\text{Br}_{14}\text{O}_2$ . Calculated, %: C 21.23; H 0.55.

#### REFERENCES

- Shishkin, V.N., Tarasova, I.V., and Butin, K.P., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 2005, p. 2305.
- Tarasova, I.V., *Cand. Sci. (Chem.) Dissertation*, Nizhnii Novgorod, 2006.
- Handbook of Organopalladium Chemistry for Organic Synthesis*, Negishi, E.-i. and de Meijere, A., Eds., New York: Wiley, 2002.
- Tao, W., Nesbitt, S., and Heck, R.F., *J. Org. Chem.*, 1990, vol. 55, p. 63.
- Bong, D.T.-Y., Gentric, L., Holmes, D., Matzger, A.J., Scherhad, F., and Vollhardt, K.P.S., *Chem. Commun.*, 2002, p. 278.
- Sonogashira, K., Tohda, Y., and Hagihara, N., *Tetrahedron Lett.*, 1975, p. 4467.
- Lu, J., Ho, D.M., Volelaar, N.J., Kraml, C.M., and Pascal, R.A., *J. Am. Chem. Soc.*, 2004, vol. 126, p. 11168.
- Furuyama, E. and Fudzi, Yu., *J. Synth. Org. Chem., Jpn.*, 1971, vol. 29, p. 92; *Ref. Zh., Khim.*, 1971, no. 16Zh162.
- Vartanyan, R.S., Kazaryan, Zh.V., and Kucherov, V.F., *Arm. Khim. Zh.*, 1974, vol. 24, p. 295.
- Qwist, W. and Wikman, H., *Acta Acad. Abo., Math. Phys.*, 1959, p. 1.
- Deacon, G.B., Farguharson, G.J., and Miller, J.M., *Aust. J. Chem.*, 1977, vol. 30, p. 1013.