

LETTERS  
TO THE EDITOR

To the 85th Anniversary of birthday of late Yu.G. Gololobov

4-(Dibromomethyl)benzaldehyde and Its Reactions  
with Primary Amines

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Received June 18, 2015

**Keywords:** 4-(dibromomethyl)benzaldehyde, trimethylphosphate, primary amines, imines

**DOI:** 10.1134/S1070363215090297

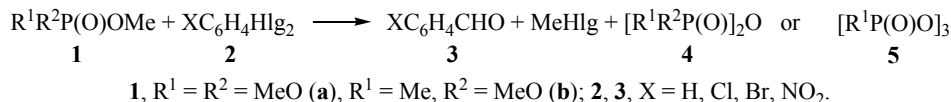
Dibromomethyl-substituted benzaldehydes contain two functional groups and are promising synthons in the synthesis of various polyfunctional organic compounds possessing valuable properties, in particular, biological activity and capability of complex formation.

Of three isomeric dibromomethyl-substituted benzaldehydes, the data are available only on 3-(dibromomethyl)benzaldehyde synthesized by the reaction of 1,3-bis(dibromomethyl)benzene with *N,N*-dimethylformamide at the temperature above 140°C. However, neither experimental procedure nor characteristics of the product are given in [1].

One of the main methods of aromatic aldehydes synthesis is the hydrolysis of dihalomethylarenes. This

method is used also in the synthesis of phthalic aldehydes. In particular, terephthalic aldehyde is prepared by the hydrolysis of 1,4-bis(dibromomethyl)benzene [2]. This method has many technological drawbacks, like a large consumption of sulfuric acid creating aggressive acid medium, corrosion of apparatus, and formation of a large amount of hydrogen bromide, which must be removed in a vacuum thus increasing the time of the process and limiting the load of the apparatus.

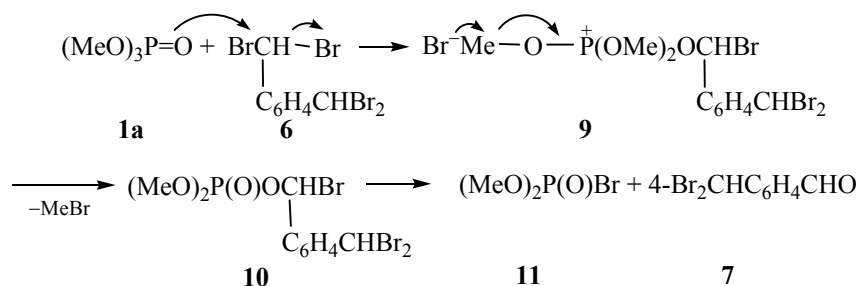
Earlier, we have found a new reaction of methyl esters of phosphorus(IV) acids **1** with dichloro- and di-bromomethylarenes **2** leading to the formation of aldehydes **3** and pyrophosphoric compounds P(IV) **4** and **5** [3, 4].



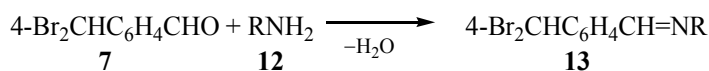
The main advantage of this method is the retention of the hydrolytically labile groups in the reaction product. Therefore, we decided to use this method for the synthesis of the earlier unknown 4-(dibromomethyl)benzaldehyde **7** from 1,4-bis(dibromomethyl)benzene **6**. We expected that with a specified ratio of compounds **1** and **6** it would be possible to retain one dibromomethyl groups. We have developed the method of copreparation of 4-(dibromomethyl)benz-

aldehyde **7** and terephthalic aldehyde **8** by the reaction of tetrabromide **6** with trimethylphosphate **1a**, which is the most commercially available of the methyl esters of P(IV) acids. The reaction was monitored by <sup>1</sup>H NMR spectroscopy. The ratios of reagents **1a** and **6** of 1.5 : 1 and 2.1 : 1 were found to be optimal and leading to the mixture of compounds **7** and **8** in the ratio 4 : 1 and 1 : 19 respectively. Under these conditions tetrabromide **6** was lacking in the reaction

Scheme 1.



Scheme 2.



**12, 13**, R = *i*-Pr (**a**), C<sub>6</sub>H<sub>4</sub>OMe-4 (**b**), CH<sub>2</sub>CH(OEt)<sub>2</sub> (**c**), (CH<sub>2</sub>)<sub>3</sub>CH(OEt)<sub>2</sub> (**d**).

mixture. On heating the mixture of compounds **1a** and **6** taken in the above ratios at 180°C for 5.5 and 21 h, respectively, the doublet of the methoxy group at phosphorus atom at 3.79 ppm (<sup>3</sup>J<sub>PH</sub> = 11.0 Hz) was practically absent in the reaction mixture. The polymeric phosphoric anhydride formed is insoluble in conventional organic solvents, so the mixture of products **7** and **8** was extracted with boiling isooctane and the individual compounds were obtained by column chromatography with benzene as an eluent.

Apparently, generation of the aldehyde group from the dibromomethyl group occurs by the mechanism of Scheme 1.

The nucleophilic attack of the phosphoryl oxygen on the methane carbon results in the release of a bromide anion and the formation of the quasi-phosphonium salt **9**, which is stabilized according to the scheme of the second stage of the Arbuzov–Michaelis reaction. The bromosubstituted ester **10** formed is unstable and decomposes with the formation of aldehyde **7** and bromophosphate **11**. The reaction of the latter with trimethylphosphate and intermediate compounds having the methoxy group at the P(IV) atom results in the polymeric phosphoric anhydride.

The 4-(dibromomethyl)benzaldehyde **7** obtained was brought in the reaction with primary amines and aminoacetals **12** in benzene in the presence of molecular sieves. After removal of solvent in a vacuum, imines **13** were obtained in high yields (Scheme 2).

The presence of dibromomethyl and acetal groups in compounds **13c** and **13d** makes them potential synthons for the synthesis of new derivatives.

In conclusion, by the reaction of trimethylphosphate with 1,4-bis(dibromomethyl)benzene we have first synthesized 4-(dibromomethyl)benzaldehyde, which was further converted to the imines, including those containing the additional acetal group.

**Reaction of trimethylphosphate 1a with 1,4-bis(dibromomethyl)benzene 6.** *a.* A mixture of 4.2 g (0.03 mol) of trimethylphosphate **1a** and 8.44 g (0.02 mol) of 1,4-bis(dibromomethyl)benzene **6** was heated at 180°C for 5.5 h, then extracted with isooctane, and the mixture of compounds **7** and **8** was isolated. Separation by column chromatography (eluent — benzene) gave 2.34 g (42%) of compound **7** as colorless crystals of mp 89–90°C. <sup>1</sup>H NMR spectrum, δ, ppm: 6.63 s (1H, CHBr<sub>2</sub>), 7.67–7.93 m (4H, C<sub>6</sub>H<sub>4</sub>), 10.02 s (1H, CHO). <sup>13</sup>C NMR spectrum, δ<sub>C</sub>, ppm: 39.49 (CHBr<sub>2</sub>), 127.35 and 130.06 (CH<sub>arom</sub>), 137.04 and 147.39 (C<sub>arom</sub>), 191.11 (CHO). Mass-spectrum, *m/z* (*I*<sub>rel</sub>, %): 247 (0.13) [*M* – CHO]<sup>+</sup>, 197 (91.3) [*M* – Br]<sup>+</sup>, 168 (7.8) [C<sub>7</sub>H<sub>5</sub>Br]<sup>+</sup>, 89 (100.0) [C<sub>7</sub>H<sub>5</sub>]<sup>+</sup>, 63 (77.5) [C<sub>5</sub>H<sub>3</sub>]<sup>+</sup>, 50 (20.4) [C<sub>4</sub>H<sub>2</sub>]<sup>+</sup>. Found, %: C 34.36; H 2.12; Br 57.41. C<sub>8</sub>H<sub>6</sub>Br<sub>2</sub>O. Calculated, %: C 34.57; H 2.18; Br 57.50. Column chromatography gave also 0.64 g (24%) of dialdehyde **8** as colorless crystals with mp 115–116°C (mp 115–116°C [2]). <sup>1</sup>H NMR spectrum, δ, ppm: 8.04 s (4H, C<sub>6</sub>H<sub>4</sub>), 10.12 s (2H, CHO). Found, %: C 71.42; H 4.45. C<sub>8</sub>H<sub>6</sub>O<sub>2</sub>. Calculated, %: C 71.63; H 4.52.

*b.* A mixture of 2.94 g (0.021 mol) of trimethylphosphate **1a** and 4.22 g (0.01 mol) of 1,4-bis(dibromomethyl)benzene **6** was heated at 180°C in the course of 21 h, extracted with isooctane, and 0.96 g (72%) of compound **8** was isolated as colorless crystals of mp 115–116°C.

**Reaction of 4-(dibromomethyl)benzaldehyde 7 with isopropylamine 12a.** A mixture of 0.5 g (1.8 mmol) of 4-(dibromomethyl)benzaldehyde, 0.11 g (1.8 mol) of isopropylamine and 0.2 g of molecular sieves 3A in 10 mL of anhydrous benzene was kept for 24 h at room temperature and filtered. After removal of solvent, 0.44 g (77%) of *N*-isopropyl-4-(dibromomethyl)benzenecarbimine **13a** was obtained as a yellow oily substance. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.25 d (6H, CHMe<sub>2</sub>, <sup>3</sup>J<sub>HH</sub> 6.3 Hz), 3.49 and 3.55 t (1H, CHMe<sub>2</sub>, <sup>3</sup>J<sub>HH</sub> 6.3 Hz), 6.61 s (1H, CHBr<sub>2</sub>), 7.55 and 7.72 d (4H, C<sub>6</sub>H<sub>4</sub>, <sup>3</sup>J<sub>HH</sub> 8.5 Hz), 8.25 s (1H, CH=N). <sup>13</sup>C NMR spectrum,  $\delta$ <sub>C</sub>, ppm: 24.17 (Me), 40.45 (CHBr<sub>2</sub>), 61.80 (NCH), 126.81 and 128.29 (CH<sub>arom</sub>); 126.81, 130.05, 137.86 and 143.63 (C<sub>arom</sub>), 157.0 (CH=N). Mass-spectrum, *m/z* (*I*<sub>rel</sub>, %): 317 (1.0) [*M*]<sup>+</sup>, 302 (16.2) [*M* - CH<sub>3</sub>]<sup>+</sup>, 276 (0.32) [*M* - C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>, 238 (100.0) [*M* - Br]<sup>+</sup>, 223 (38.5) [*M* - CH<sub>3</sub>Br]<sup>+</sup>, 182 (1.4) [C<sub>8</sub>H<sub>7</sub>Br]<sup>+</sup>, 168 (9.4) [C<sub>7</sub>H<sub>5</sub>Br]<sup>+</sup>, 144 (24.7) [*M* - CH<sub>3</sub>Br<sub>2</sub>]<sup>+</sup>, 117 (22.6) [C<sub>8</sub>H<sub>7</sub>N]<sup>+</sup>, 103 (11.1) [C<sub>7</sub>H<sub>5</sub>N]<sup>+</sup>, 89 (61.9) [C<sub>7</sub>H<sub>5</sub>]<sup>+</sup>, 43 (55.3) [C<sub>3</sub>H<sub>7</sub>]<sup>+</sup>. Found, %: C 41.16; H 4.03; Br 49.95. C<sub>11</sub>H<sub>13</sub>Br<sub>2</sub>N. Calculated, %: C 41.41; H 4.11; Br 50.09.

***N*-(4-Methoxyphenyl)-4-(dibromomethyl)benzenecarbimine (13b)** was prepared similarly from 0.25 g (0.9 mmol) of 4-(dibromomethyl)benzaldehyde and 0.11 g (0.9 mmol) of 4-methoxybenzenamine. Yield 0.35 g (100%), yellow crystals, mp 120–123°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 3.82 s (3H, OMe), 6.64 s (1H, CHBr<sub>2</sub>), 6.87 and 7.18 d (4H, C<sub>6</sub>H<sub>4</sub>OMe, <sup>3</sup>J<sub>HH</sub> 9.1 Hz), 7.63 and 7.88 d (4H, C<sub>6</sub>H<sub>4</sub>CHBr<sub>2</sub>, <sup>3</sup>J<sub>HH</sub> 7.8 Hz), 8.44 s (1H, CH=N). Found, %: C 46.79; H 3.29; N 3.51. C<sub>15</sub>H<sub>13</sub>Br<sub>2</sub>NO. Calculated, %: C 47.02; H 3.43; N 3.65.

***N*-(2,2-Diethoxyethyl)-4-(dibromomethyl)benzenecarbimine (13c)** was obtained from 0.5 g (1.8 mmol) of 4-(dibromomethyl)benzaldehyde and 0.24 g (1.8 mmol) of 2,2-diethoxyethanamine. Yield 0.65 g (93%), yellow crystals, mp 34–35°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.15 t (6H, OCH<sub>2</sub>Me, <sup>3</sup>J<sub>HH</sub> 7.0 Hz), 3.56 quintet and 3.71 quintet (4H, OCH<sub>2</sub>Me, <sup>3</sup>J<sub>HH</sub> 7.0 Hz), 3.76 d (1H, NCH<sub>2</sub>, <sup>3</sup>J<sub>HH</sub> 5.2 Hz), 4.77 t (1H, CHO<sub>2</sub>, <sup>3</sup>J<sub>HH</sub> 5.2 Hz), 6.63 s (1H, CHBr<sub>2</sub>), 7.59 d and 7.72 d (4H, C<sub>6</sub>H<sub>4</sub>, <sup>3</sup>J<sub>HH</sub> 8.4 Hz), 8.26 s (1H, CH=N). <sup>13</sup>C NMR spectrum,  $\delta$ <sub>C</sub>, ppm: 15.45 (OCH<sub>2</sub>Me), 40.08 (CHBr<sub>2</sub>), 62.45 (NCH<sub>2</sub>), 64.60 (OCH<sub>2</sub>Me), 101.89 (CHO<sub>2</sub>), 126.80 and 128.39 (CH<sub>arom</sub>), 137.48 and 143.91 (C<sub>arom</sub>), 161.70 (CH=N). Mass-spectrum, *m/z* (*I*<sub>rel</sub>, %): 346 (0.73) [*M* - C<sub>2</sub>H<sub>5</sub>O]<sup>+</sup>, 318 (0.29) [*M* - C<sub>4</sub>H<sub>9</sub>O]<sup>+</sup>, 302 (0.07) [*M* - C<sub>4</sub>H<sub>9</sub>O<sub>2</sub>]<sup>+</sup>, 288 (0.43) [*M* - C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>, 268 (2.4) [*M* - C<sub>2</sub>H<sub>4</sub>OBr]<sup>+</sup>, 261 (0.4) [C<sub>8</sub>H<sub>7</sub>Br<sub>2</sub>]<sup>+</sup>, 238 (1.0) [*M* - C<sub>4</sub>H<sub>10</sub>OBr]<sup>+</sup>, 209 (2.2) [*M* - C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>Br]<sup>+</sup>, 197 (1.8) [*M* - C<sub>6</sub>H<sub>11</sub>O<sub>2</sub>Br]<sup>+</sup>,

182 (4.7) [C<sub>8</sub>H<sub>7</sub>Br]<sup>+</sup>, 130 (6.1) [C<sub>6</sub>H<sub>12</sub>O<sub>2</sub>N]<sup>+</sup>, 103 (100.0) [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>, 75 (63.8) [C<sub>3</sub>H<sub>7</sub>O<sub>2</sub>]<sup>+</sup>. Found, %: C 42.53; H 4.79; Br 40.51; N 3.44. C<sub>14</sub>H<sub>19</sub>Br<sub>2</sub>NO<sub>2</sub>. Calculated, %: C 42.77; H 4.88; Br 40.65; N 3.56.

***N*-(4,4-Diethoxybutyl)-4-(dibromomethyl)benzenecarbimine (13d)** was prepared similarly from 0.5 g (1.8 mmol) of 4-(dibromomethyl)benzaldehyde and 0.32 g (1.8 mmol) of 4,4-diethoxybutanamine. Yield 0.72 g (92%), yellow oily compound. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.21 t (6H, OCH<sub>2</sub>Me, <sup>3</sup>J<sub>HH</sub> 7.0 Hz), 1.43–1.80 m (4H, CH<sub>2</sub>CH<sub>2</sub>), 3.20–3.70 m (6H, OCH<sub>2</sub>, NCH<sub>2</sub>), 4.43 t (1H, CHO<sub>2</sub>, <sup>3</sup>J<sub>HH</sub> 5.0 Hz), 6.59 s (1H, CHBr<sub>2</sub>), 7.52 d and 7.68 d (4H, C<sub>6</sub>H<sub>4</sub>, <sup>3</sup>J<sub>HH</sub> 8.0 Hz), 8.20 s (1H, CH=N). Found, %: C 46.71; H 5.69; N 3.13. C<sub>17</sub>H<sub>25</sub>Br<sub>2</sub>NO<sub>2</sub>. Calculated, %: C 46.91; H 5.80; N 3.22.

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Tesla BS-567A (100 MHz) and Bruker AVANCE 400WB (400.13 and 100.61 MHz) instruments in CDCl<sub>3</sub>. Chromatomass-spectrometric analysis was performed on a DFS instrument (Thermo Electron Corporation, Germany) in the electron impact mode. Experimental conditions: energy of ionizing electrons 70 eV, ion source temperature 250°C; capillary column BPX5 SGE (32 mm × 50 m), carrier gas helium. For compound **13c**, the direct inlet system was used. The temperature of ampule-evaporator was varied from 50 to 350°C. Mass-spectral data were treated by the use of Xcalibur program. The peaks of ions with <sup>79</sup>Br isotope are given.

#### ACKNOWLEDGMENTS

This work was performed with the financial support from the Ministry of Education and Science of RF within the framework of the basic part of State contract no. 2014/56.

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