

LETTERS
TO THE EDITORNew Method of Synthesis
of Functionally Substituted Aromatic AldehydesM. B. Gazizov*, S. Yu. Ivanova, Sh. N. Ibragimov,
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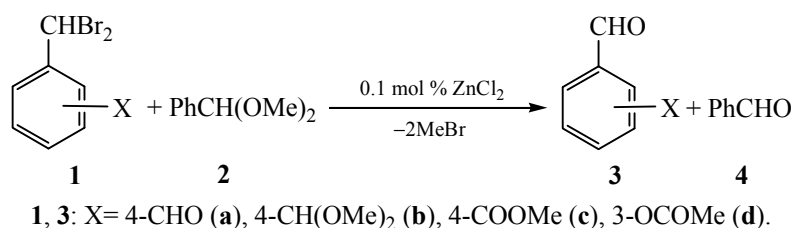
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We have previously carried out for the first time the reaction of methyl esters of P(IV) acids with dihalomethylarenes resulting in the formation of aromatic aldehydes and P(IV) pyro-compounds [1, 2]. The main disadvantages of this method are high temperature (160–180°C) and high cost of P(IV) acids esters. In the last decade two promising method of aromatic monoaldehydes preparation from dihalomethylarenes have been developed: heating a mixture of dihalomethylarenes with a large excess of dimethyl sulfoxide [3] or

pyridine [4] at 70–120°C for 1–18 h followed by treating the reaction mixture with water. However, isolation of pure aldehydes is labor consuming.

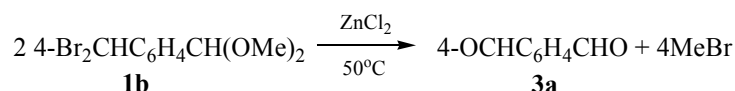
We suggest for the first time to synthesize functionally substituted aromatic aldehydes via catalytic debromomethoxylation of dibromomethylarenes **1** with the use of benzaldehyde dimethyl acetal **2**. Zinc chloride being a soft Lewis acid was used as a catalyst, which did not form a stable complex with the aldehyde group.



Some experiments showed that a catalyst-free reaction between compounds **1** and **2** occurs only at 220°C. The reaction was complete in 2 h at 50°C and 1 h at 80°C when using 0.1 mol % of ZnCl₂. It was carried out in the solvent-free conditions.

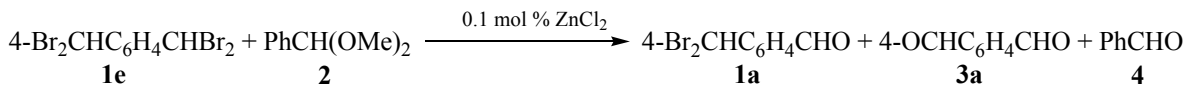
During the reaction such important functional groups as methoxycarbonyl and carbonyl were not affected. Acetal moieties of dibromide **1b** and 4-(dime-

thoxymethyl)benzenecarbaldehyde **3b** were involved into debromomethoxylation, and the major reaction product was terephthalaldehyde **3a**. Compound **3b** was detected only by ¹H NMR and chromatography methods. Moreover, since compound **1b** contains both dibromomethyl and acetal groups, we expected their intermolecular interactions. Indeed, the formation of terephthalaldehyde **3a** with 96% yield occurred when adding catalytic amounts of ZnCl₂ to compound **1b**.



Generally, depending on the reactant ratio the reaction of tetrabromide **1e** with benzaldehyde dimethyl acetal **2** may result in the formation of three

aldehydes: monoaldehyde **1a**, dialdehyde **3a**, and benzaldehyde **4**. Tetrabromide **1d** might not react completely.



In the ^1H NMR spectrum of the reaction mixture (**1e** : **2** = 1.0 : 2.1) there was no signal at 6.61 ppm corresponding to the proton of dibromomethyl group. Terephthalaldehyde **3a** was isolated in 90% yield.

In order to apply this reaction to the synthesis of 4-(dibromomethyl)benzenecarbaldehyde **1a** [5] we varied the reactants ratio. At a ratio of 1.0 : 1.5, tetrabromide **1e** was absent in the reaction mixture (according to ^1H NMR). Compounds **1a** and **3a** were isolated in pure state by column chromatography eluting with benzene with the yields of 11 and 64%, respectively. Thus, in the absence of tetrabromide **1e** in the reaction mixture the main reaction product was terephthalaldehyde **3a**, i. e., the second dibromomethyl group of **1e** was affected, and the yield of **1a** was small.

However, when the ratio of the reagents of 1 : 1, 17.7% of the starting tetrabromide **1e** can be isolated. The yields of chromatographically isolated products **1a**, **3a**, and **4** reached 22.6, 53.2, and 40.5%, respectively. Hence, when using the equimolar reactants ratio the yields of the target compound **1a** can be increased 2 times.

The starting acetal **2** was easily regenerated by treating the formed benzaldehyde with trimethyl orthoformate.

In summary, we developed for the first time the method of the synthesis of functionally substituted aromatic aldehydes by catalytic debromomethoxylation of dibromomethylarenes using benzaldehyde dimethyl acetal.

The reaction of 1,4-bis(dibromomethyl)benzene 1e with benzaldehyde dimethyl acetal 2. *Ratio of 1.0 : 2.1.* *a.* A mixture of 3 g (0.007 mol) of tetrabromide **1e**, 2.28 g (0.015 mol) of acetal **2**, and 0.1 g (0.0007 mol) of zinc chloride was heated at 50°C for 2 h. Extraction with isooctane yielded 0.8 g (84%) of compound **3a** as colorless crystals melting at 115–116°C (mp 115–116°C [6]). The mother liquor yielded 0.41 g (28%) of benzaldehyde **4**.

b. A mixture of 3 g (0.007 mol) of tetrabromide **1e**, 2.28 g (0.015 mol) of acetal **2**, and 0.1 g (0.0007 mol) of zinc chloride in 5 mL of isooctane was heated at 50°C for 2.5 h. Isooctane solution was decanted, and the residue was further extracted with 10 mL of isooctane. Compound **3a** (0.85 g, 89%) was isolated from the combined isooctane solutions. The mother liquor yielded 0.43 g (29%) of benzaldehyde **4**.

c. A mixture of 3 g (0.007 mol) of tetrabromide **1e**, 2.28 g (0.015 mol) of acetal **2**, and 0.1 g (0.0007 mol) of zinc chloride in 5 mL of isooctane was heated at 80°C for 1 h. Compound **3a** (0.86 g, 90%) was isolated from the combined isooctane solutions. The mother liquor yielded 0.4 g (28%) of benzaldehyde **4**.

d. Ratio of 1.0 : 1.5. A mixture of 3 g (0.007 mol) of tetrabromide **1e**, 1.67 g (0.011 mol) of acetal **2**, and 0.1 g (0.0007 mol) of zinc chloride in 5 mL of isooctane was heated at 80°C for 1 h. Isooctane solution provided 0.5 g (53%) of compound **3a**. The residue was chromatographed (eluent – benzene) to give 0.66 g (55%) of benzaldehyde **4**, 0.22 g (11%) of compound **1a**, and 0.11 g (11%) of compound **3a**.

The reaction of 4-(dibromomethyl)benzenecarbaldehyde 1a with acetal 2. A mixture of 1 g (0.0036 mol) of compound **1a**, 0.58 g (0.0038 mol) of acetal **2** and 0.049 g (0.00036 mol) of zinc chloride in 5 mL isooctane was heated at 80°C for 1 h. Compound **3a** (0.4 g (83%)) was isolated from isooctane solution. The mother liquor yielded 0.21 g (55%) of benzaldehyde **4**.

The reaction of 1-(dibromomethyl)-4-(dimethylmethoxymethyl)benzene 1b with acetal 2. A mixture of 1 g (0.0031 mol) of compound **1b**, 0.5 g (0.0033 mol) of acetal **2**, and 0.04 g (0.00031 mol) of zinc chloride was heated at 50°C for 1.5 h. Compound **3a** (0.15 g, 36%) was isolated by extraction with isooctane. The mother liquor was chromatographed (eluent benzene : ether = 19 : 1) to provide fractions containing 0.1 g (30%) of benzaldehyde **4**, 0.06 g (15%) of dialdehyde **3a**, as well as a fraction consisting of compounds **2** and **3b**, which were detected by TLC (Sorbfil, benzene).

Transformation of 1-(dibromomethyl)-4-(dimethylmethoxymethyl)benzene 1b into dialdehyde 3a under the action of catalytic amounts of zinc chloride. A mixture of 1.1 g (0.0034 mol) of compound **1b** and 0.046 g (0.00034 mol) of zinc chloride was heated at 50°C for 1 h. Extraction with isooctane allowed isolating 0.44 g (96%) of compound **3a**.

Methyl-4-formylbenzenecarboxylate (3c). A mixture of 1 g (0.0032 mol) of compound **1c**, 0.52 g (0.0034 mol) of acetal **2**, and 0.044 g (0.00032 mol) of zinc chloride was heated at 50°C for 2 h and then at 80°C for 2 h. Extraction with isooctane provided 0.43 g (82%) of compound **3c** as colorless crystals melting at 59–61°C (mp 63–65°C [7]). ¹H NMR spectrum (CDCl₃), δ, ppm: 2.42 s (3H, CH₃), 7.47–8.13 m (4H, C₆H₄), 10.08 s (1H, CHO). Benzaldehyde **4** (0.1 g, 29%) was isolated from mother liquor.

3-Formylphenyl acetate (3d). A mixture of 2 g (0.0065 mol) of compound **1d**, 1.4 g (0.0068 mol) of acetal **2**, and 0.09 g (0.00065 mol) of zinc chloride was heated at 80°C for 2 h. The reaction mixture was chromatographed eluting with benzene–diethyl ether mixture (19 : 1). Yield 0.33 g (30%), oil [8]. ¹H NMR spectrum (CDCl₃), δ, ppm: 2.42 s (3H, CH₃), 7.47–8.13 m (4H, C₆H₄), 10.08 s (1H, CHO). In addition, 0.2 g (29%) of benzaldehyde was isolated. ¹H NMR spectra were recorded on a Tesla BS-567A and AVANCE 400WB instruments operating at 100 and 400.13 MHz. Chemical shifts were reported relative to TMS using the residual proton signals of the solvent as internal reference.

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