J. prakt. Chem. 336 (1994) 260–262

Journal für praktische Chemie
Chemiker-Zeitung

Brominative Deoxygenation of Some Aldehydes and Ethers

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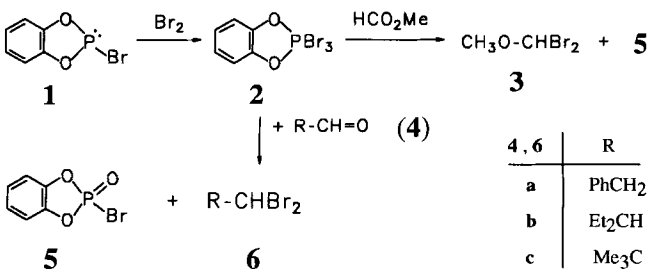
Received May 3rd, 1993

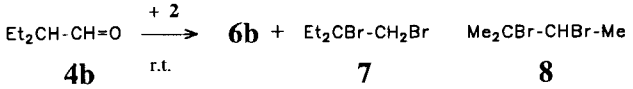
Abstract. Three aldehydes (**4a–c**) are transformed into 1,1-dibromides (**6a–c**) by 2,2,2-tribromo-2,2-dihydro-1,3,2-benzodioxaphosphole (**2**). This reagent (**2**) is also very active in the cleavage of ethers; its reactions may show some features of carbonium as well as of S_N2 character.

H. Gross and coworkers [1–3] described preparations of the catechyl phosphorus tribromide (**2**) from the monobromide **1** and of the α,α-dibromo ether **3** from methyl formate with **2**; they have also reported [2, 3] the application of **2** and **3** in some C–O bond cleavage reactions. We have recently shown [4, 5] that substitution of a ketonic oxygen atom by bromine may be accomplished conveniently either with the tribromophosphole **2** of with the less reactive reagent **3**. Extension of this brominative deoxygenation to aldehydes **4** could be useful because the expected 1,1-dibromo derivatives **6** possess synthetic significance [6, 7]; but only heptanal has been converted into 1,1-dibromoheptane [7] with **2**, whereas chloral [8] and fluoral [9] were reported to react by addition rather than by substitution. For a comparison of this procedure with other known methods we chose to study only the three test compounds **4a–c** because these represent "difficult" cases for reasons of ready polymerization (of **4a**), too many side-products (with **4c** [10, 11]), partial rearrangement (with **4c** [6, 10]) or complete rearrangement (with **4b** [6]). For example, the dibromide **6b** is unknown because the bis(trifluoromethylsulfonyl) acylal of 2-ethylbutanal (**4b**) gave only the rearranged dibromide **7** [6].



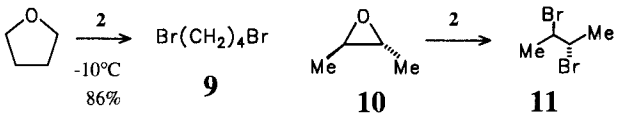
Phenylacetaldehyde (**4a**) reacted quickly with the tribromide reagent **2** to give 75 % of 1,1-dibromo-2-phenylethane (**6a**) and 21 % of E- and Z-β-bromostyrene. This one-step conversion is simpler than the literature procedures [6, 12] but proceeds less cleanly. On the other hand, 2-ethylbutanal (**4b**) afforded **6b** (17 %) and only 19 % of the rearrangement product **7**. The formation of **7** indicates some carbonium character of the reaction, as noticed before [5], and was not supressed when the reaction was run in the presence of tetraethylammonium bromide (0.3 equiv.) in chloroform.

The starting aldehydes **4a** (ca. 5 %) and **4b** (ca. 19 %) were found in the crude products even though the conversions had been complete (by in-situ ^{1}H-NMR), as observed before [5] with ketones. However, α-bromination [5] did not occur with these aldehydes, and the application of reagent **3** was therefore unnecessary. The purification of **6b** was achieved by selective destruction of **7** with potassium tert-butoxide, whereas several other methods failed, like treatment of **6b/7** with triethylamine, sodium iodide in hot acetone, $ZnCl_2$/cons. HCl, zinc dust, or hot aqueous methanol [13] or ethanol.



The sterically shielded pivalaldehyde (**4c**) produced a mixture of **6c** (39 %), **8** (32 %) and 2,4,6-tri-tert-butyl-1,3,5-trioxane (26 % yield, predominantly the isomer with C_3 symmetry by NMR). The latter was certainly formed [14] under the action of traces of HBr which contaminate the reagent **2** if prepared in situ [5]; since it did not change upon further heating with **2**, the present procedure is not very productive for **6c**. Nevertheless, the rearrangement product **8** could be destroyed with potassium tert-butoxide to leave the highly volatile 1,1-dibromide **6c** (14 %). Pure **6c** has been obtained only twice [7, 15], and our preparation is presently surpassed solely by the simple one-step reaction of **4c** with triphenyl phosphite and bromine [7].

The suitability of acetals [2] in place of their aldehydes or ketones was examined in two cases. Cyclopentanone diethylacetal [16] (without $ZnCl_2$ [2]) was indeed transformed into 1-bromocyclopentene [5] (46 %) and bromoethane; initial cooling was necessary, and 1,1-dibromocyclopentane was not formed, in contrast to the reaction of cyclopentanone [5] with **2**. Therefore, the mechanistic details must be somewhat different for conversion of the acetal as compared to cyclopentanone. However, the dimethyl acetal of phenylacetaldehyde yielded a mixture of (Z)-β-methoxystyrene (^{1}H NMR [17]), and unidentified olefinic compounds without any trace of the β-bromostyrenes. Butyl-vinylether as an acetal equivalent decomposed with **2** but formed no trace of bromoethylene.



Saturated ethers were cleaved very quickly by reagent **2**, and indeed much easier than by dibromo-triphenylphosphorane [18, 19] or by gaseous hydrogen bromide [20]. Diethyl ether afforded two equivalents of bromoethane, and 1,4-dibromobutane (**9**) was formed from THF [19, 20] in high yield with only one equivalent of **2**. In a brief search for the stereochemical features of this brominative deoxygenation, we were somewhat surprised to discover that trans-2,3-dimethyloxirane (racemic **10**) was transformed with extreme facility by **2** into meso-2,3-dibromobutane [21] (**11**, identified by ^{13}C-NMR [22]) in the presence or absence of 0.6 equivalents of tetraethylammonium bromide. Hence this transformation is stereoselective and involves an odd number of configurational inversions, perhaps via a bromonium intermediate as one possibility. Reagent **3** required 3 d at room temperature for consumption of the oxirane **10**, forming initially the racemic diastereoisomer of **11** and later also the meso compound **11** together with methyl bromide and other products.

This rather cursory investigation suggests that the tribromide **2** and its successor reagent **3** may be useful in many further applications [1–3]. Compared to known alternative preparations, the one-step method described here is convenient and somewhat less prone to rearrangement but inferior to the literatur method [7] for **6c**.

We gratefully acknowledge support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Experimental

Equipment, solvents and the improved preparation of the monobromide **1** have been described [5].

Brominative Deoxygenation Reaction of Some Aldehydes and Ethers

General Procedure

A dried 2-necked flask (25 ml), bearing a two-way (Y) adapter with a gas inlet, was fitted with a thermometer and a pressure-equalizing dropping funnel carrying a $CaCl_2$ tube. A magnetic stirring bar, the monobromide **1** (2.30 ml, 18.2 mmol) and anhydrous, ethanol-free CH_2Cl_2 or $CHCl_3$ (4.0 mol) were introduced under N_2. The solution was stirred in an ice-bath, elemental bromine (0.87 ml, 17.0 mmol) was added dropwise, and stirring continued at room temperature for 15 min. With external cooling the substrate (15 mmol in 4 ml of solvent) was added slowly, and the mixture was stirred for 2 h at room temperature. The workup procedure [5] was slightly modified for the products **6a–c** from aldehydes by adding pentane (30 ml) rather than CH_2Cl_2 to the flask. The cooled contents were poured onto ice-cold 2N Na_2CO_3 solution (40 ml) and stirred for 15 min. After phase separation the aqueous layer was extracted with more pentane (2 × 20 ml). The combined pentane layers were washed with 2N NaOH (3 × 20 ml) and distilled water (20 ml), then dried with $CaCl_2$ and concentrated at a cautiously controlled pressure.

1,1-Dibromo-2-phenylethane (**6a**)

Phenylacetaldehyde (**4a**, 1.755 ml, 15.0 mmol) was treated with reagent **2** in CH_2Cl_2 according to the general procedure. The crude product (3.047 g) was purified by short chromatography on silica gel (10 g) with light petroleum ether (150 ml) to give 2.463 g of a 78:22 mixture of **6a** and the β-bromostyrenes (E and Z); total yield 62 %. – ^{1}H NMR (CCl_4): as in Lit. [6, 12]

1,1-Dibromo-2-ethylbutane (**6b**)

2-Ethylbutanal (**4b**, 1.50 g, 15 mmol) was added dropwise to reagent **2** in chloroform according to the general procedure such that the internal temperature remained below 25 °C. The raw material (2.54 g) contained 17 % of **6b** together with 19 % of 3-bromo-3-(bromomethyl)-pentane (**7**), 19 % of regenerated **4b**, and unidentified side-products. ^{1}H NMR (CCl_4) of **7**: as in Lit. [6].

Since separation of **6b** from **7** could not be achieved by distillation or chromatography, the mixture was heated to 80°C with potassium tert-butoxide (2.25 g) in tert-butylalcohol (10 ml) at a reflux condenser for 2 h. This cooled solution was poured into distilled water (50 ml) and extracted with ether (3 × 15 ml). The combined ether layers were washed, dried with $CaCl_2$, and evaporated at a controlled pressure. After chromatography of a sample on silica gel with light petroleum ether the colourless liquid **6b** was too volatile to give a suitable combustion analysis which, however, showed the correct C/H ratio for $C_6H_{12}Br_2$. IR (film): ν = 2965, 2935, 2877, 1465, 1165, 677 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.97 (t, ^3J = 7.5 Hz, 2 CH_3), 1.48 (m, 2 H), 1.66 (mc, 3 H), 5.96 (d, ^3J = 2.7 Hz, $CHBr_2$); ^{1}H NMR (CCl_4): δ = 5.85 (d, ^3J = ca. 2 Hz, $CHBr_2$); ^{13}C NMR ($CDCl_3$): δ = 11.7 (2 CH_3), 24.4 (2 CH_2), 53.0 and 53.8 (2 CH); MS (35 eV, room temp.): As published [6] for the isomer **7**. $C_6H_{12}Br_2$ (244.0): Calcd. C 29.54, H 4.96; found C 32.09, H 5.17.

1,1-Dibromo-2,2-dimethylpropane (**6c**)

As described for **6b**, 2,2-dimethylpropanal (**4c**, 1.64 ml, 15.0 mmol) was added to reagent **2** in chloroform solution. The pen-

tane extracts were evaporated at 40 °C/160 Torr to leave 2.345 g of crude product containing **6c** (39 %), **8** (32 %) and the trioxane (26 %). ^{1}H NMR (CCl_4) of 2,3-dibromo-2-methylbutane (**8**): as in Lit. [10].
2,4,6-Tri-tert-butyl-1,3,5-trioxane, ^{1}H NMR (CCl_4): δ = 1.08 (s, 9 H), 5.80 (s, 1 H); ^{13}C NMR ($CDCl_3$): δ = 26.0 (3 CH_3), 38.1 (3 q-C), 101.1 (3 CH).
Pure **6c** (492 mg, 14 %) was obtained by treatment with potassium tert-butyloxide (see **6b**), chromatography on silica gel with light petroleum ether, and final distillation as a colourless liquid at 90–100 °C (bath temp.)/50 Torr (Lit. [6] 81–82 °C/50 Torr; Lit. [7] 50–52 °C/15 Torr). ^{1}H NMR (CCl_4): as in Lit. [6, 10, 11]; MS (70 eV): as in Lit. [11] but (M^+–1) much weaker.

1,4-Dibromobutane (**9**)

Tetrahydrofuran (3.24 ml, 42.2 mmol) was added dropwise to a solution of reagent **2** (40 mmol) in anhydrous chloroform (20 ml) under Ar at –78 °C. The exothermic reaction was controlled by cautious warming and re-cooling as necessary. After stirring at room temperature overnight and workup [5], pure **9** (7.42 g, 86 %) was isolated by distillation: Bp. 73–77 °C/10 Torr (Lit. [20] 198 °C/760 Torr); ^{1}H NMR ($CDCl_3$): δ = 2.01 (m, 4 H), 3.39 (m, 4 H).

2,3-Dibromobutane (**11**)

trans-2,3-Butenoxide (**10**, 3.50 ml, 39 mmol) was added to a precooled solution of reagent **2** (40 mmol) in anhydrous chloroform (30 ml). The exothermic reaction was started by warming up with intermittent cooling and was finished in 2 h at room temperature. The workup [5] yielded pure meso-**11** (at least 3.59 g, 42 %) by distillation: Bp. 41–42 °C/12 Torr; m.p. ca. –26 °C(Lit. [21] –24 °C); ^{1}H NMR (CCl_4): δ = 1.85 (m, 6 H), 4.10 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ = 25.3 (q, CH_3), 54.1 (d, CHBr), compare Lit. [22].

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