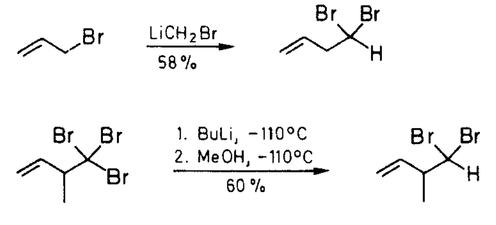
Conversion of Aldehydes into 1,1-Dibromoalkanes

R.W. Hoffmann,* P. Bovicelli
Fachbereich Chemie der Philipps-Universität, Hans-Meerwein-Strasse, D-3550 Marburg, Federal Republic of Germany

Aliphatic and aromatic aldehydes have been converted into 1,1-dibromoalkyl derivatives using a 1:1 mixture of triphenyl phosphite and bromine as reagent.

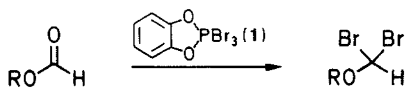
In connection with our interest in stereoselective formation of bromocarbenoids from 1,1-dibromoalkanes,[1] we realized that 1,1-dibromoalkanes are accessible by only a few methods.The most prominent method is the alkylation[2] or hydroxyalkylation[3] of lithium dibromomethanide[4] (Scheme A).



Scheme A

Alternatively tribromomethyl compounds can be reduced[5] to dibromomethyl compounds, the starting materials are easily accessible e.g. by free radical addition reactions. Both of these reaction sequences are ones in which dibromomethyl groups are introduced with C—C bond formation. A refunctionalization scheme, in which the carbon skeleton is not altered, would therefore be a desireable alternative. Hence we became interested in a direct conversion of aldehydes into 1,1-dibromoalkanes.

At present there is only one isolated example of such a transformation using phosphorus dibromide trichloride (PCl_3Br_2).[6] This reagent and phosphorus pentabromide (PBr_5) have previously been used in the conversion of ketones to geminal dibromoalkanes.[7] Aromatic aldehydes were converted into dibromomethyl derivatives with boron tribromide (BBr_3).[8] A related transformation of formate esters into dibromomethyl ethers has been achieved using catechol–phosphorane tribromide (**1**).[9] This appears to be a more reactive reagent (Scheme **B**).



Scheme **B**

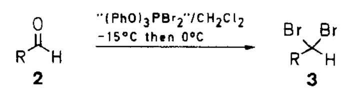
For this reason we tested its reactivity towards heptanal (**2a**) at room temperature. This way we obtained a 50% yield of 1,1-dibromoheptane (**3a**). However, much better yields were obtained with a 1:1 mixture of triphenylphosphite/bromine, while no conversion could be realized using dibromotriphenylphosphorane[10] (Scheme C).

Reagent	Yield (%)
Ph_3PBr_2	0
1	40
"$(PhO)_3PBr_2$"	70

Scheme C

The mixture of triphenyl phosphite/bromine is not a homogeneous reagent.[11] It rather is predominantly a 70:30 mixture of bromotetraphenoxyphosphorane [$(PhO)_4PBr$] and phosphorous tribromide (PBr_3). After testing other ratios of triphenyl phosphite and bromine, as well as the addition of Lewis acids, or of an excess of sodium bromide, we adopted the reaction of an aldehyde with this 1:1 mixture of triphenyl phosphite and

Table. 1,1-Dibromoalkanes **3** Prepared



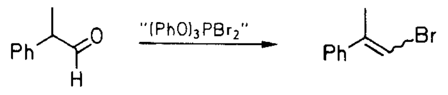
Product	R	Yield (%)	mp (°C) or bp (°C)/Torr	Molecular Formula[a] or Lit. bp (°C)/Torr
3a	n-C_6H_{13}	70	67–70/15	$C_7H_{14}Br_2$ (258.0)
3b	CH(Me)(Pr)	56	76–78/15	$C_6H_{12}Br_2$ (244.0)
3c	c-C_6H_{11}	55	60–61/0.3	$C_7H_{12}Br_2$ (256.0)
3d	t-Bu	50	50–52/15	$C_5H_{10}Br_2$ (230.1)
3e	$BnOCH_2$	64	–[b]	$C_9H_{10}Br_2O$ (294.0)
3f	Ph	76	104–106/15	108–109/6[14]
3g	3-O_2N,4-ClC_6H_3	91	74–75	$C_7H_4Br_2ClNO_2$ (329.4)
3h	(S)-CH(Me)(OBn)[c]	62	–[b]	$C_{10}H_{12}Br_2O$ (308.0)

[a] Satisfactory microanalyses obtained **3a–e**, **h**: C ±0.38, H ±0.09; **3g**: C ±0.18, H ±0.24, N ±0.10.
[b] Not determined.
[c] The enantiomeric excess (ee) of **3h** was 99.4% indicating that no racemization had taken place.

bromine at − 15 °C for the conversions reported in the Table.

In this way a variety of 1,1-dibromoalkanes were obtained in acceptable yields. However, the reaction mixture contains a strong Lewis acid. This may be the reason for the decomposition on attempted reaction of fufural, acrolein, *O*-isopropylideneglyceraldehyde, 2-(dibenzylamino)-3-phenylpropanal, or citronellal with triphenyl phosphite/bromine.

The 2-phenylpropionaldehyde **4** was converted by this reagent into an *E*/*Z*-mixture of the vinyl bromides **5** rather than the desired 1,1-dibromoalkane (Scheme **D**).



4 5

Scheme **D**

These results delineate the limitations of the present transformation. We were pleased, however, that the (*S*)-2-benzyloxypropionaldehyde **2h** could be converted into the dibromo derivative **3h** without noticeable racemization.

Triphenyl phosphite, bromine, heptanal, 2-methylpentanal, cyclohexanecarbaldehyde, 2,2-dimethylpropanal, and 4-chloro-3-nitrobenzaldehyde were purchased from Merck-Schuchardt company. (−)-(*S*)-Benzyloxypropanal was prepared following the procedure of Hanessian.[12] All aldehydes were used freshly distilled. Temperatures quoted are not corrected. NMR-spectra were measured using a Bruker AC-300 spectrometer. Microanalyses were obtained using a Hereaus element analyser. Rotations were measured using a Perkin-Elmer polarimeter 241.

(−)-(*S*)-2-Benzyloxy-1,1-dibromopropane (3h); Typical Procedure: Bromine, (1.92 g, 12 mmol) is added dropwise to a cold solution (0 °C) of triphenyl phosphite (3.72 g, 12 mmol) in dry CH_2Cl_2 (6 mL). The solution remains colorless until 3 mmol of bromine are added. Then it turns from yellow to red. This solution is cooled to − 15 °C. Subsequently a solution of (−)-(*S*)-2-benzyloxypropanal (**2h**; 1.0 g, 6.1 mmol) in CH_2Cl_2 (0.5 mL) is added dropwise to give a light yellow to colorless solution. After warming to 0 °C basic alumina (1.5 g) is added. The mixture is filtered over basic alumina (4 g) with Et_2O (3 × 20 mL). The solvent is evaporated and the crude product is chromatographed on a column (12 cm × 3 cm) of silica gel (230–400 mesh) eluting with petroleum ether (bp 40–60 °C)/Et_2O, 9:1. The resulting (−)-(*S*)-2-benzyloxy-1,1-dibromopropane (**3h**); is obtained as a colorless oil; yield: 1.17 g, (62 %); $[\alpha]_D^{18}$ − 8.21° (c = 2.68, CH_2Cl_2).

The enantiomeric purity of **3h** was determined to 99.4 % by gas chromatography using heptakis[3-*O*-(N-isopropylcarbamoyl)-2,6-di-*O*-pentyl]-β-cyclodextrin as a chiral stationary phase.

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.37 (d, 3 H, J = 6.1 Hz, CH_3), 3.75 (dq, 1 H, J = 3.5, 6.1 Hz, CH), 4.62, 4.57 (2d, 2 H, J = 11.8 Hz, OCH_2), 5.71 (d, 1 H, J = 3.5 Hz, $CHBr_2$), 7.2–7.31 (m, 5 H_{arom}).

^{13}C-NMR ($CDCl_3$/TMS): δ = 16.7, 49.4, 71.8, 78.8, 127.8, 127.9, 128.5, 137.5.

1,1-Dibromoheptane (**3a**):

Following the typical procedure heptanal (**2a**, 5.6 g, 49 mmol) is converted into 1,1-dibromoheptane and purified by distillation; yield: 8.8 g (70 %).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.91 (t, 3 H, J = 6.8 Hz, CH_3), 1.2–1.35 (m, 6 H, CH_2), 2.39 (dt, 2 H, J = 6.25, 8.9 Hz, $\underline{CH_2}$-$CHBr_2$), 5.71 (t, 1 H, J = 6.25 Hz, $CHBr_2$).

^{13}C-NMR ($CDCl_3$): δ = 14.0, 22.5, 27.9, 28.0, 31.5, 45.5, 46.3.

1,1-Dibromo-2-methylpentane (**3b**):

Following the typical procedure 2-methylpentanal (**2b**, 5.0 g, 50 mmol) is converted into 1,1-dibromo-2-methylpentane which is purified by distillation; yield: 6.83 g (56 %).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.91 (t, 3 H, J = 6.94 Hz, CH_3), 1.11 (d, 3 H, J = 6.51 Hz, $\underline{CH_3}CH$), 1.26–1.5 (m, 4 H, CH_2), 2.02–2.08 (m, 1 H, CH), 5.82 (d, 1 H, J = 2.79 Hz, $CHBr_2$).

^{13}C-NMR ($CDCl_3$/TMS): δ = 14.0, 16.5, 20.0, 36.4, 44.4, 55.4.

1,1-Dibromomethylcyclohexane (**3c**):

Following the typical procedure cyclohexanecarbaldehyde (**2c**, 630 mg, 5.6 mmol) is converted into 1,1-dibromomethylcyclohexane which is purified by chromatography using petroleum ether (bp 40–60 °C) as eluent; yield: 788 mg (55 %).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.12–1.37 (m, 6 H $(CH_2)_3$), 1.6–1.7 (m, 1 H, CH), 1.8–2.0 (m, 4 H, $-\underline{CH_2}CH\underline{CH_2}-$), 5.72 (d, 1 H, J = 3.8 Hz, $CHBr_2$), cf. Ref.[6].

^{13}C-NMR ($CDCl_3$/TMS): δ = 2.6, 25.9, 30.0, 49.2, 54.6.

1,1-Dibromo-2,2-dimethylpropane (**3d**):

Following the typical procedure pivalaldehyde (**2d**, 4.3 g, 50 mmol) is converted into **3d** obtained by distillation; yield: 5.75 g (50 %).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.12 (s, 9 H, CH_3), 5.57 (s, 1 H, $CHBr_2$).

^{13}C-NMR ($CDCl_3$/TMS): δ = 26.7, 39.7, 61.6.

2-Benzyloxy-1,1-dibromoethane (**3e**):

Following the typical procedure (benzyloxy)acetaldehyde[13] (**2e**, 0.80 g, 5.3 mmol) is converted into 2-benzyloxy-1,1-dibromoethane obtained by chromatography eluting with petroleum ether (bp 40–60 °C)/Et_2O (9:1); yield: 1.0 g (64 %).

^{1}H-NMR ($CDCl_3$/TMS): δ = 3.99 (d, 2 H, J = 6.2 Hz, OCH_2), 4.69 (s, 2 H, $PhCH_2O$), 5.66 (t, 1 H, J = 6.2 Hz, $CHBr_2$), 7.33–7.41 (m, 5 H_{arom}).

^{13}C-NMR ($CDCl_3$/TMS): δ = 42.2, 73.4, 76.4, 127.8, 128.1, 128.5, 137.1.

α,α-Dibromotoluene (**3f**):

Following the typical procedure benzaldehyde (**2f**, 5.3 g, 50 mmol) is converted into α,α-dibromotoluene which is obtained by chromatography with petroleum ether (bp 40–60 °C) as eluent; yield: 9.46 g (76 %).

^{1}H-NMR ($CDCl_3$/TMS): δ = 6.67 (s, 1 H, $CHBr_2$), 7.3–7.4 (m, 3 H_m,H_p), 7.59 (dt, 2 H, J = 6.6, 1.7 Hz, H_o).

^{13}C-NMR ($CDCl_3$/TMS): δ = 41.0, 126.5, 128.6, 129.8, 141.9.

α,α-Dibromo-4-chloro-3-nitrotoluene (**3g**):

Following the typical procedure 4-chloro-3-nitrobenzaldehyde (**2g**, 1.85 g, 10 mmol) is converted into α,α-dibromo-4-chloro-3-nitrotoluene obtained by chromatography eluting with petroleum ether (bp 40–60 °C)/Et_2O (2:1); yield: 3.0 g (91 %).

^{1}H-NMR ($CDCl_3$/TMS): δ = 6.65 (s, 1 H, $CHBr_2$), 7.61 (d, 1 H, J = 8.4 Hz, H-5), 7.78 (dd, 1 H, J = 8.4, 2.3 Hz, H-6), 8.12 (d, 1 H, J = 2.3 Hz, H-2).

^{13}C-NMR ($CDCl_3$/TMS): δ = 36.8, 123.7, 128.3, 131.2, 132.4, 141.8, 147.0.

We would like to thank Prof. W. A. König, Hamburg, for determining the enantiomeric purity of **3h** *by gas chromatography. This study was supported by the Fonds der Chemischen Industrie. P. B. thanks the Conciglio Nationale delle Ricerche of Italy for a fellowship.*

Received: 19 February 1990; revised: 22 March 1990

(1) Hoffmann, R. W.; Bewersdorf, M.; Ditrich, K.; Krüger, M.; Stürmer, R. *Angew. Chem.* **1988**, *100*, 1232; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1176.
Hoffmann, R. W.; Julius, M. *J. Organomet. Chem.* **1988**, *353*, C30.

(2) Villieras, J.; Bacquet, C.; Normant, J.-F. *Bull. Soc. Chim. Fr.* **1975**, 1797.

(3) Taguchi, H.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1588.

(4) Köbrich, G.; Fischer, R.H. *Chem. Ber.* **1968**, *101*, 3208.

(5) Villieras, J.; Rambaud, M. *Synthesis* **1980**, 644.
The example shown is from Mikolaiski, W., unpublished results, Marburg 1989.

(6) Kropp, P.J.; Pienta, N.J. *J. Org. Chem.* **1983**, *48*, 2084.

(7) Hawkins, B.L.; Bremser, W.; Borcic, S.; Roberts, J.D. *J. Am. Chem. Soc.* **1971**, *93*, 4472.
Kabe, Y.; Takata, T.; Ueno, K.; Ando, W. *J. Am. Chem. Soc.* **1984**, *106*, 8174.

(8) Lansinger, J.M.; Ronald, C. *Synth. Commun.* **1979**, *9*, 341.

(9) Gross, H.; Karsch, U. *J. Prakt. Chem.* **1965**, *29*, 315.
Gloede, J. *Z. Chem.* **1982**, *22*, 126.

(10) Attempts to convert pentanal into 1,1-dibromopentane using other reagents such as tungsten hexabromide (WBr_6) or thionyl bromide ($SOBr_2$) were unsuccesful. Treatment of 1-bromo-1-(trimethylsiloxy)pentane with $SOBr_2$ resulted in ca. 40–50% of 1,1-dibromopentane; Schlapbach, A., unpublished results, 1987.

(11) Tseng, C.K. *J. Org. Chem.* **1979**, *44*, 2793.

(12) Hanessian, S.; Kloss, J. *Tetrahedron Lett.* **1985**, *26*, 1261.

(13) Corbet, J.-P.; Benezra, C. *J. Org. Chem.* **1981**, *46*, 1141.

(14) Hine, J.; Lee, D.E. *J. Am. Chem. Soc.* **1951**, *73*, 22.