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LETTERS

Synthesis of 1,1-dibromo-1-alkenes from partially and unprotected aldoses

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Abstract—Partially and unprotected aldoses react with dibromomethylenetriphenylphosphorane, generated in situ from dibromomethyltriphenylphosphonium bromide in the presence of zinc, to give corresponding unsaturated Wittig adducts in good yields.

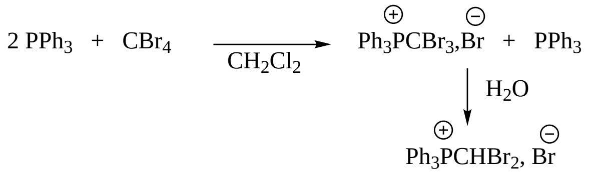
1,1-Dibromo-1-alkenes are versatile intermediates in organic synthesis. These dibromocompounds have been often used for the synthesis of acetylenics[1,2] and more recently in coupling reactions.[3]

The Wittig-type reaction[4,5] has been employed as a convenient method to their synthesis and the well-known conditions are the Corey–Fuchs conditions.[1] Recently, Rassat[6] described the synthesis of acetylenics via 1,1-dibromo-1-alkenes from aromatic and aliphatic aldehydes. These dibromocompounds were prepared by the condensation of aldehydes with dibromomethylenetriphenylphosphorane generated in situ from dibromomethyltriphenylphosphonium bromide[4,7] and *t*BuOK. Moreover Chapleur[8] described the synthesis of 1,1-dibromo-1-alkenes from lactones. In this case, the dibromomethylenetriphenylphosphorane was generated by reaction of *t*BuOK in THF on an excess of bromomethyltriphenylphosphonium bromide.

In a preceding communication, we reported the reaction of partially and unprotected aldoses with methyl bromoacetate or bromoacetonitrile, tri-*n*-butylphosphine and zinc, to give the corresponding E unsaturated Wittig products with good yields and stereoselectivity.[9]

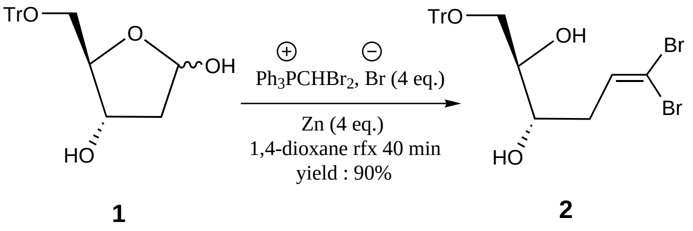
We have extended the use of zinc to generate in situ the dibromomethylenetriphenylphosphorane in order to synthesize 1,1-dibromo-1-alkenes from aldoses whereon there are few reports.

We now report herein an efficient method for olefination of aldoses having free hydroxyl groups to 1,1-dibromo-1-alkenes precursors of glyco-1-ynitols. The reaction of 2-deoxy-5-*O*-trityl-D-ribofuranose **1** with dibromomethyltriphenylphosphonium bromide in the presence of zinc in refluxing 1,4-dioxane led to (2*R*,3*R*) 6,6-dibromo-1-*O*-trityl-hex-5-ene-1,2,3-triol **2** (Scheme 1).



$$2\,PPh_3 + CBr_4 \xrightarrow[CH_2Cl_2]{} Ph_3\overset{\oplus}{P}CBr_3,\overset{\ominus}{Br} + PPh_3 \xrightarrow{H_2O} Ph_3\overset{\oplus}{P}CHBr_2,\ \overset{\ominus}{Br}$$

Scheme 2.



Scheme 1.

Keywords: dibromoalkenes; aldoses; dibromomethyltriphenylphosphonium bromide; ylid.

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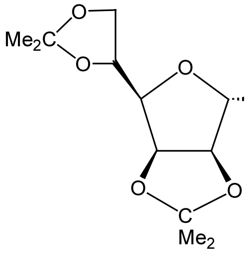
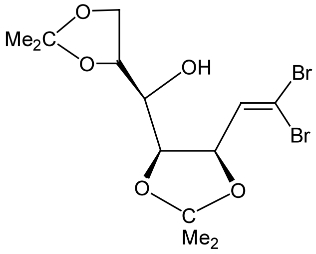
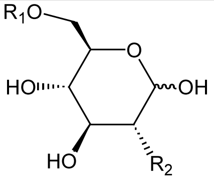
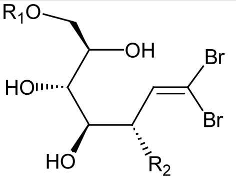
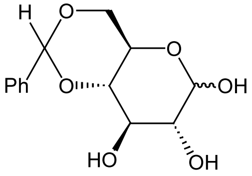
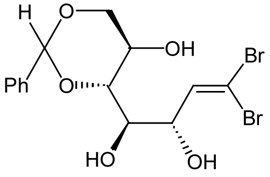
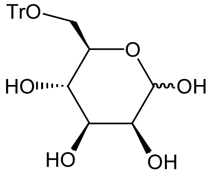
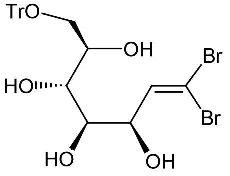
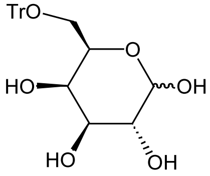
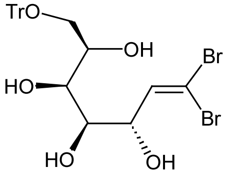
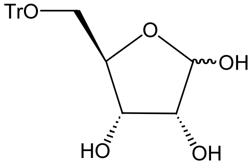
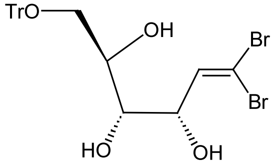
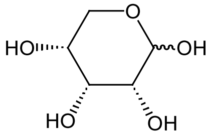
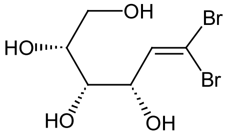
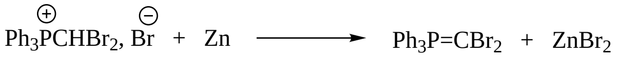
Table 1. Reaction of partially and unprotected aldoses with dibromomethyltriphenylphosphonium bromide (4 equiv.) in presence of zinc (4 equiv.) in refluxing 1,4-dioxane

Substrates	t(min)	Olefins	Yields *
 **3**	65	 **4**	*90%*
 **5** R_1 : Tr, R_2 : H **7** R_1 : Tr, R_2 : OH **9** R_1 : H, R_2 : H	65 60 50	 **6** R_1 : Tr, R_2 : H **8** R_1 : Tr, R_2 : OH **10** R_1 : H, R_2 : H	*63%* *55%* *60%*
 **11**	50	 **12**	*60%*
 **13**	100	 **14**	*76%*
 **15**	90	 **16**	*44%*
 **17**	45	 **18**	*77%*
 **19**	30	 **20**	*48%*

*: Isolated yields.

NMR and mass were used to establish the structure of olefin **2**. Indeed, the NMR spectra exhibited three characteristic peaks: 134.8 and 90.5 ppm attributed, respectively to C-$_{5}$ and C-$_{6}$ and 6.48 ppm attributed to H-$_{5}$.

Good yields of **2** were obtained using a fourfold excess of dibromomethyltriphenylphosphonium bromide[10] and a fourfold excess of zinc.[11] This phosphonium salt was obtained under a modified Ramirez procedure[4,10] (Scheme 2) and isolated. Moreover it must be recrystal-



$$Ph_3\overset{\oplus}{P}CHBr_2, \overset{\ominus}{Br} + Zn \longrightarrow Ph_3P{=}CBr_2 + ZnBr_2$$

Scheme 3.

lized and its structure has been confirmed by NMR and mass.[10] When zinc's activation is not sufficient, the reaction needs a larger excess of both reagents to bring it to completion. The zinc needs to be prepared by the oxydo-reduction reaction of zinc chloride by lithium or sodium.

A series of dibromoolefins has been obtained under our optimized conditions (Table 1): the yields were excellent with 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **3** (90%), and slightly lower with partially and unprotected substrates (44 to 77%). These yields are satisfactory on the free aldoses: 60% from deoxy-D-glucose **9** and 48% from D-ribose **19**. On the other substrates, a deprotection of hydroxyl groups takes place when the reaction time is too long. This degradation was attributed to the formation of $ZnBr_2$ during the reaction. Under Rassat's conditions: dibromomethyltriphenylphosphonium bromide with *t*BuOK in THF, the dibromoolefins cannot be formed from aldoses when a free hydroxyl group is present. But, it is possible on the 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **3**, to obtain olefin **4** in similar yield (89%).

The mildness of our conditions allowed us to form the dibromoolefins on aldoses having free hydroxyl groups. This is due to the formation of the dibromomethylenetriphenylphosphorane in situ from the corresponding phosphonium salt and zinc (Scheme 3). In this way, usual Wittig's parasite reactions were avoided.

In summary, an easy direct access to 1,1-dibromo-1-alkenes derivatives from partially or unprotected aldoses is now available. At present, we continue our studies to synthesize acetylenics from these 1,1-dibromoolefins.

General procedure for the preparation of 1,1-dibromo-1-alkenes

The anhydrous 1,4-dioxane (15 mL) was added to a mixture of zinc (3.19 mmol, 4 equiv.), dibromomethyltriphenylphosphonium bromide (3.19 mmol, 4 equiv.) and sugar (0.79 mmol). The mixture was stirred under an argon atmosphere and allowed to 60°C to reflux. When the substrate had completely reacted (TLC), the mixture was filtered and concentrated in vacuum to afford a residue, which was purified by flash chromatography.

Acknowledgements

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10. *Preparation of dibromomethyltriphenylphosphonium bromide*: carbon tetrabromide* (16.4 g, 49.4 mmol) was added to a solution of triphenylphosphine (26 g, 99.1 mmol) in methylene chloride (240 mL). The solution was stirred for 15 min at room temperature. Water (8 mL) was added to this resulting red reaction. After 15 min of vigorous magnetic stirring, the aqueous layer was separated of CH_2Cl_2. The organic layer was dried and evaporated at reduced pressure to syrup. The salt was precipitated by addition of acetonitrile. The yellow powder obtained was filtered, dried under vacuum and recrystallized from dry acetonitrile** at 20 h at reflux temperature. The solution was filtered hot and the dibromomethyltriphenylphosphonium bromide *** recrystallized was filtered and dried under vacuum.
    *: CBr_4 must be a colorless solid.
    **: Acetonitrile must be freshly distillate on $CaCl_2$.
    ***: The salt was stable at least 6 months if stored at −20°C under an inert atmosphere.
    NMR ^{13}C ($CDCl_3$, 75 MHz): 30.12 (d, $J=48$ Hz), 116.70 (d, $J=87.7$ Hz), 130.68 (d, $J=12.8$ Hz), 134.98 (d, $J=9.8$ Hz), 136.40 (d, $J=2$ Hz). FAB-MS (nitrobenzylalcohol matrix): $C_{19}H_{16}Br_2P^+$ *m/z*: 433, $C_{19}H_{15}BrP^+$ *m/z*: 353, $C_{19}H_{16}P^+$ *m/z*: 275.
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