USE OF TETRABUTYLAMMONIUM BOROHYDRIDE AND ITS CHLORO DERIVATIVES FOR THE SELECTIVE REDUCTION OF SOME ACETALS AND ALDEHYDES

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The possible use of tetrabutylammonium borohydride and its chloro derivatives for the selective reduction of polyfunctional compounds was studied in the present paper. It is known that borohydrides are very efficient, mild, and selective reducing agents for aldehydes that contain other functional groups (epoxide, ester, lactone, nitrile, etc.).

When fumaraldehyde acetal $(CH_3O)_2CHCH = CHCHO$ (I), which contains an aldehyde and an acetal group, and also an α,β double bond, is reduced by Bu_4NBH_4 (IIa), $Bu_4NBH_2Cl_4$ (IIb) or Bu_4NBHCl_3 (IIc) in various solvents (THF, CH_2Cl_2 , C_6H_6), in the range from -5 to 20°C, the starting aldehyde underwent complete tarring.

In order to ascertain the effect of the α,β double bond on the reduction of the aldehyde and the acetal group we studied the reaction of citral oxide (III), malonaldehyde bis(diethyl acetal) (IV), and crotonaldehyde diethyl acetal (V) with (IIa) and (IIb):



It proved that the reduction of (III) by either (IIa) or (IIb) proceeds with retention of the oxide ring and leads to epoxygeraniol (VI), which is found to agree with the data given in [1] on the reduction of (III) by $NaBH_4$.

When diacetal (IV) is treated with either (IIb) or (IIc), it is reduced to 1,3-diethoxypropane $C_2H_5OCH_2$ -CH₂CH₂OC₂H₅ (VII). Such progress of the reaction can serve to explain the known fact that the alumohydrides or borohydrides of the alkali metals in admixture with the Lewis acids AlCl₃ or BF₃ [2-5] cause the reductive cleavage of saturated acetals, in which connection the yield of the formed ethers increases with increase in the amount of Al or B halides added to the reaction relative to the complex hydrides. The reaction of the complex hydrides with Lewis acids probably leads to replacement of hydride hydrogen by halogen atoms and the formation of halo-substituted alumo- and borohydrides, which evidently are the reagents for the reductive cleavage of acetals. Such an assumption is also supported by the fact that (IIa) does not reduce (IV).

Like in the case of (I), only tarring of the starting product occurred when (V) is reduced by (IIb) in various solvents and at different temperatures.

As a result, the presence of a double bond, conjugated with either an aldehyde or an acetal group, prevents the reduction of α , β -unsaturated aldehydes and acetals using the chloro derivatives of tetrabutylammonium borohydrides.

The treatment of 1-formyl-2,2-dichloro-3-methylcyclopropane diethyl acetal (VIII) with (IIa) in either THF or C_6H_6 gave a mixture of several products (GLC) with close retention times. Reduction using (IIb) led to 1,1-dichloro-2-(ethoxymethyl)-3-methylcyclopropane (IX):



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TABLE 1. Yields and Characteristics of Obtained Products

Compound	Yield,	bp, °C (p, mm Hg)	n ²⁰ _D	PMR spectrum (δ, ppm, J, Hz)
(VI)	47	118120(8) *	1,4655 *	1,22 d (3H, CH ₃ , $J=2$); 1,55 s, 1,64 s (6H, (CH ₃) ₂ C=); 1,8-1,2 m(4H, CH ₂ CH ₂); 2,5-2,9 m(1H, CH _{cycl}); 3,4-4,0 m(3H, CH ₂ OH): 4,9-5,2 m(1H, CH=)
(VII)	35	67-68(50)†	1,4115 †	1.08 t (6H, 2CH ₃ , $J=7$); 1,65 q (2H, CH ₂ , J=6); 3,31 t (4H, 2CH ₂ O, $J=7$); 3,35 t (4H, 2CH ₂ O, $J=6$)
(IX) ‡	88	75-77 (15)	1,4505	1,15 t (3H, CH ₃ ether, $J=7$); 1,2–1,4 m(5H, CH ₃ , 2H _{cycl}); 3,30–3,55 m(4H, 2CH ₂ O)

*Cf. [1].

†Cf. [7].

‡ Found: C 45.83; H 6.97; Cl 38.94%. $C_7H_{12}Cl_2O$. Calculated: C 45.92; H 6.65; Cl 38.73%.

The structure of the obtained compounds was proved by the elemental analysis and PMR spectra. The purity of the obtained products was verified by GLC.

EXPERIMENTAL

The GLC analysis was run on an LKhM-8 MD-5 chromatograph, using a flame-ionization detector, nitrogen as the carrier gas, and a 1.4 m \times 0.003 m glass column packed with 5% SE-30 deposited on Chromaton N-AW-DMCS. The PMR spectra were recorded on a Varian DA-60-IL instrument (60 MHz), using CCl₄ as the solvent and TMS as the internal standard, while the chemical shifts are given on the δ scale.

The starting (IIb) and (IIc) were obtained as described in [6].

Epoxygeraniol (VI). a) With sittring, to a suspension of 9.9 g of (IIa) in 100 ml of abs. benzene at $5-7^{\circ}$ was added in 30-40 min a solution of 6.6 g of (III) in 30 ml of abs. benzene, after which the mixture was brought up to ~20° and kept for 5 h. Then the reaction mixture was added to a 3:1 acetone-water mixture, cooled to -5° to 0°, brought up to ~20° and stirred for 3-4 h. The organic layer was separated, while the aqueous layer was extracted with ether. The combined organic extract was dried over K_2CO_3 , the solvent was evaporated in a rotor evaporator, and the residue was distilled.

b) To 26.6 g of (IIb) in 100 ml of abs. benzene was added at 5° a solution of 6.6 g of (III) in 50 ml of abs. benzene, and then the mixture was warmed up to $\sim 20^{\circ}$ and kept for a day. Then the reaction mixture was poured into an alcohol solution of caustic, cooled to 0° , and stirred for 3 h. Water was added and the organic layer was separated.

The aqueous layer was extracted with ether. The combined organic fractions were dried over K_2CO_3 , the solvent was removed in a rotor evaporator, and the residue was distilled. The yield and characteristics of (IV) are given in Table 1.

<u>General Method for Reduction of (I), (IV), (V), and (VIII)</u>. With stirring, to a suspension of 0.025 mole of (IIa-c) in 50 ml of abs. benzene at $0-5^{\circ}$ was added in drops a solution of 0.025 mole of (I), (IV), (V), or (VIII) in 30 ml of abs. benzene. The mixture was gradually heated to $65-70^{\circ}$ and then kept at this temperature for 6 h. Then most of the solvent was evaporated in vacuo using a water-jet pump until a precipitate began to deposit. The obtained concentrated solution was treated with pentane and the precipitate was filtered and washed with pentane. The combined pentane extracts were dried over Na₂SO₄, the solvent was removed, and the residue was distilled. The yields and characteristics of the obtained products (VI), (VII), and (IX) are given in Table 1.

CONCLUSIONS

1. The reduction of citral oxide using tetrabutylammonium borohydride and its chloro derivatives proceeds with retention of the oxide ring and leads to epoxygeraniol.

2. The chloro derivatives of tetrabutylammonium borohydride can be used for the reductive cleavage of saturated acetals.

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PREPARATION OF HALO-SUBSTITUTED ESTERS OF CARBOXYLIC ACIDS

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It is known that cyclic ethers when treated with hydrogen halides and the anhydrides and acid halides of carboxylic acids undergo cleavage at the C-O bond to give halo-substituted esters [1-3], which can be used as plasticizers and intermediates in the synthesis of detergents, alcohols, amines, and quaternary ammonium salts.

Methods were described in [4-6] for cleaving THF by carboxylic acids in the presence of inorganic acid halides and Lewis acids as the catalysts. As a rule, the reaction is run by heating the reaction mixture for a long time above 100°C. The use of a catalyst hinders the isolation of the desired product.

We obtain the 4-chlorobutyl esters of carboxylic acids by refluxing THF, the carboxylic acid, and either $SOCl_2$ or $POCl_3$ at 65° for 4-6 h and then keeping the reaction mixture at room temperature. The reaction products distilled completely as the pure compounds, except 4-chlorobutyl acetate, which contained up to 30% of high-boiling unidentified products:

 $\begin{array}{c} \operatorname{R}(\operatorname{CH}_2)_n\operatorname{COOH} + \underbrace{\swarrow}_{O} \xrightarrow{\operatorname{SOCl}_2(\operatorname{POCl}_2)} \operatorname{R}(\operatorname{CH}_2)_n\operatorname{COO}(\operatorname{CH}_2)_4\operatorname{Cl} \\ (\operatorname{Ia-c}) & (\operatorname{IIa-c}) \\ \operatorname{R} = \operatorname{H}, \ n = 1 \ (a); \ \operatorname{R} = \operatorname{Cl}, \ n = 1 \ (b); \ \operatorname{R} = \operatorname{Br}, \ n = 2 \ (c). \end{array}$

Apparently, $SOCl_2$ and $POCl_3$ first react with the carboxylic acids to give the acid chlorides (III) and HCl:

$$(Ia-c) + SOCl_2(POCl_3) \rightarrow R(CH_2)_nCOCl + HCl$$

(IIIa-c)

The HCl cleaves THF via the intermediate carbonium cation [7] to give 4-chlorobutanol (IV):

$$\overbrace{O}^{\text{HCl}} \overbrace{OH \ Cl^{\Theta}}^{\text{HCl}} \rightarrow \text{HO}(CH_2)_4 \text{Cl (IV)}$$

The acylation of (IV) by acid chloride (III) leads to ester (II). The cleavage of the THF ring by a proton is more probable than by an acyl cation, due to more rapid and milder cleavage, than under conditions that exclude the entrance of hydrogen halides into the reaction mixture [8].

1,4-Dioxane was not cleaved under the indicated conditions after 6 h of refluxing.

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