REDUCTION OF 4-BROMO-1-METHOXYCARBONYLCUBANE WITH LITHIUM ALUMINUM HYDRIDE AND ALUMINUM HYDRIDE

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Introduction

This work continues a series of investigations dealing with reduction of cubane derivatives containing various functional groups by hydrides of light metals [1-5].

In connection with the continuous interest to cubane derivatives, as potential pharmaceuticals [6-8], and the multistage synthesis of these compounds the development of the most efficient and selective methods to modify such derivatives and to study their structures is very urgent.

One of the principal goals of this study was the development of more efficient, in comparison with an earlier known [9], method for preparing and studying a structure of 4-bromo-1-hydroxymethylcubane which can be used as an initial or intermediate compound in the synthesis of some biologically active substances, in particular, nitrates of cubane containing alcohols.

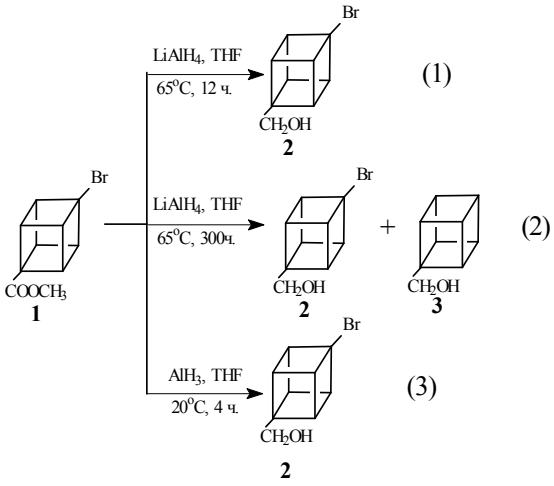
Results and Discussion

At the initial stage of the research, the reduction of ether **1** (see scheme) with lithium aluminum hydride in THF was studied.

Our attempts to increase the yield of carbinol **2** in comparison with earlier described (80 %) [9] at the reduction of this ether with lithium aluminum hydride (LAH) at higher temperature (65^{0}C), significant excess LAH (from 3:1 to 10:1) and longer duration of the process failed: the yield of carbinol **2** did not exceed 80 %, and at realization of reaction during 48-300 h it was decreased owing not only to the reduction of an ester group, but also hydrodebromination (scheme, eq.1 and 2).

With the purpose to develop a much more effective and selective method for preparing carbinol **2** we investigated the reduction of ether **1** with aluminum hydride.

It was established that the reduction of **1** by aluminum hydride proceeded under mild conditions (15-25^{o}C), much faster (4 h at 20^{0}C), than with LAH and resulted in a target product with higher yield (~94 %) (scheme, eq. 3). Besides the reduction of **1** by AlH_3 proceeded with high selectivity (hydrodebromination did not occur at the reduction of ester **1** with AlH_3 within several days).



The scheme

Carbinol **2** synthesized in our laboratory was identified on the basis of the element analyses, ^{1}H and ^{13}C NMR and IR spectra. The m. p. was 123-125^{o}C. Found (%): C, 50.92; H, 4.38; Br, 37.38. C_9H_9BrO. Calculated (%): C, 50.73; H, 4.26; Br, 37.50. The spectrum ^{1}H NMR: 1.70 (s, 1H, OH); 3.79 (s, 2H, $\underline{CH_2}OH$); 4.00 (m, 3H, $\underline{CH}CCH2$, A-part AA'A"BB'B", $\Delta\nu\approx30$); 4.18 (m, 3H, $CH_{cube}CBr$, B-part AA'A "BB'B"). The spectrum ^{13}C NMR: 45.18 (3C, $\underline{CH}_{cube}CCH_2OH$); 54.19 (3C, $\underline{CH}_{cube}CBr$); 59.12 (1C, $\underline{C}_{cube}CH_2OH$); 62.99 (1C, CH_2OH); 64.96 (1C, CBr).

The IR spectrum (KBr), ν/cm^{-1}: 3260 vs (OH); 2987 vs (CH); 2922 m, 2853 m (CH_2); 1456 w (CH_2); 1432 w (OH); 1316 m (CH); 1249 w (C-C); 1203 s (C_{cube}-Br); 1192 w, 1120 w, 1101 w (C-C); 1035 vs, 1004 s (OH); 839 m (C-C); 815 m (C-Br).

Conclusions

1. The reduction of 4-bromo-1-methoxy-carbonylcubane (**1**) with lithium aluminum hydride and aluminum hydride in THF has been investigated.
2. A new effective method for preparing 4-bromo-1-hydroxymethylcubane with a high yield that

included the reduction of **1** with aluminum hydride under mild conditions has been developed.

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