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Facile Bromination of O-Benzylidene Sugar and THP Ethers with NBS in Chloroform in the Presence of AIBN

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FACILE BROMINATION OF O-BENZYLIDENE SUGAR AND THP ETHERS WITH NBS IN CHLOROFORM IN THE PRESENCE OF AIBN

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Abstract: N-Bromosuccinimide in chloroform in the presence of a catalytic amount of AIBN is found to cleave O-benzylidene sugar into bromobenzoate in efficient manner. THP-ethers were cleaved into bromides and bromo-esters in high yield.

Free radical bromination of O-benzylidene sugars with N-bromosuccinimide (NBS) in carbon tetrachloride is a well established way of preparing bromo deoxy sugar benzoates.[1] It is also shown that the same type of reactions can be brought about with bromotrichloromethane (BTM) under u.v. irradiation.[2] As a part of our programme on synthesis of upper half of azadirachtin, a natural product isolated from neem trees, we required to prepare bromobenzoate **2**. Although reaction of **1** with NBS in CCl_4 at reflux temperature under reported conditions[3] provided the **2**

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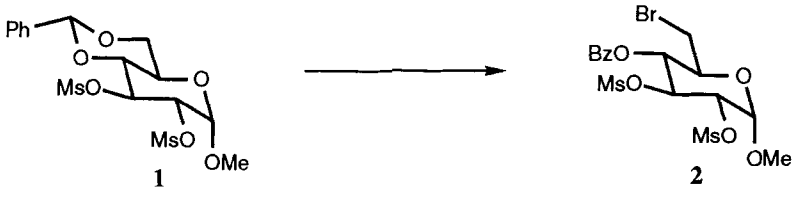
in satisfactory manner, we herein report a modified procedure for the same transformation using NBS-AIBN in chloroform. We also report a cleavage of THP ethers into bromo-esters and/or bromide under the same condition.



1 2

The reaction of the O-benzylidene sugar **1** in dry chloroform with NBS in the presence of a catalytic amount of AIBN at reflux temperature (closed system) for 15-30 min provided the bromobenzoate **2**[3] in more than 76% yield. Thus, with this modified condition the reaction time is reduced. Although there is not a major advantage with NBS-AIBN in chloroform for the transformation **1** to **2**, the polar solvent might facilitate the solubility of substrates which are sparingly soluble in CCl_4. The obvious difference is seen in the cleavage of THP ethers (Table) which are resistant with NBS (with or without AIBN) in CCl_4 even under prolong heating. The THP ether of primary alcohol is cleaved to provide δ-bromoester as the only product. But, in case of secondary THP ether, as expected, we obtained mixture of alkyl bromide and δ-bromoester where the later is in major proportion.

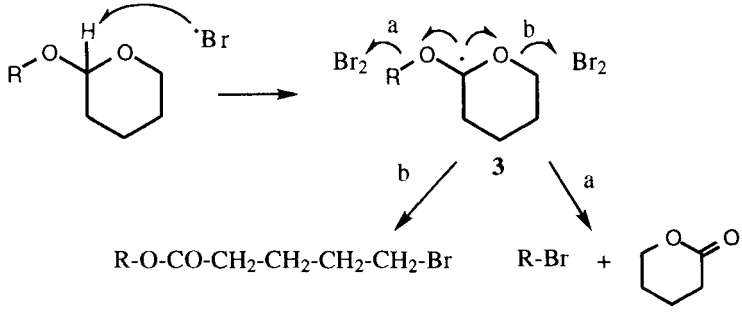
It is proposed that the reaction proceeds *via* radical intermediate **3**. The HBr formed in the reaction, by abstraction of hydrogen, reacts with NBS to produce bromine which can react with the radical intermediate **3** in two ways as shown in the scheme. Formation of ketones or aldehydes in few cases can be explained by the abstraction of the benzylic hydrogen. It is clear from the table that as the stability of benzylic radical is increased, the formation of carbonyl compound is

Table

R-OTHP $\xrightarrow[\text{reflux, 15 - 30 min}]{\text{NBS, AIBN, } CHCl_3,}$ R-O-CO-CH_2-CH_2-CH_2-CH_2-Br (**A**) + R-Br (**B**)

Entry	R	Ratio[a] of **A** & **B**	Yield for major compound (%)
1.	Me-$(CH_2)_8$-CH_2-	100 : 00	74
2.	Cyclohexyl-	86 : 14	86
3.	Menthyl-	82 : 18	80
4.	Ph-CH_2-	15 : 85	30[b]
5.	Ph-CH(Me)-	0 : 100	61[c]
6.	Ph_2-CH-	0 : 100	37[d]

[a]The ratio was determined by ^{1}H NMR analysis of the crude mixture. [b]Lower isolated yield is due to decomposition of benzyl bromide. 5% of benzaldehyde is also obatined. [c]25% of acetophenone was also isolated. [d]40% of benzophenone was also obtained.



Scheme: Mechanism for the cleavage of THP ethers

increased. Although we have not isolated the bye-product, δ-valerolactone, its presence was noticed in the ^{1}H NMR spectrum of the crude reaction mixture.

Experimental Section[4]

General Procedure: The O-benzylidene sugar **1** or THP ether (2 mmol) in dry chloroform (5 ml) was treated with NBS (2.5 mmol) in the presence of a catalytic amount of AIBN at reflux temperature (closed system) for 15-30 min (Colour of the reaction mixture changed from heterogeneous colourless to homogeneous red, and finally to homogeneous colourless). The solvent was removed on rotavap in vacuo and the crude was purified over silica gel. The **2**[3] was obtained in more than 76% yield. The THP ethers cleavage results are summarized in the table.

δ-Bromoester from decanol THP ether (entry 1): R_f 0.56 (2% EtOAc:Pet.-ether); IR (thin film) 1730 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ0.9 (t, J = 5 Hz, 3H), 1.33 (bs, 16H), 1.83 (m, 4H), 2.30 (t, J = 6.5 Hz, 2H), 3.47 (t, J = 6 Hz, 2H), 4.10 (t, J = 6.5 Hz, 2H); ^{13}C NMR (20 MHz, $CHCl_3$) δ14.0, 22.7, 23.6, 26.0, 28.7, 29.3, 29.5, 30.9, 31.7, 31.9, 32.1, 32.8, 33.4, 64.7, 173.3; FABMS m/z 321 (M^+); Anal. calcd. for $C_{15}H_{29}O_2Br$: C, 56.07; H, 9.03; O, 9.97; Found: C, 56.4; H, 9.12; O, 10.02.

δ-Bromoester from cyclohexyl THP ether (entry 2): IR (thin film) 1720 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ0.8 - 2.1 (bm, 14H), 2.3 (t, J = 6.5 Hz, 2H), 3.40 (t, J = 6 Hz, 2H), 4.63 (bm, 1H). Anal. calcd. for $C_{11}H_{19}O_2Br$: C, 50.19; H, 7.22; O, 12.17; Found: C, 50.24; H, 7.12; O, 12.42.

δ-Bromoester from menthyl THP ether (entry 3): IR (thin film) 1720 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ0.5 - 2.1 (bm, 22H), 2.3 (t, J = 6.5 H, 2H), 3.4 (t, J = 6.2 Hz, 2H), 4.62 (bm, 1H); FABMS m/z 319 (M^+). Anal. calcd. for $C_{15}H_{27}O_2Br$: C, 56.43; H, 8.46; O, 10.03; Found: C, 56.14; H, 8.42; O, 10.22.

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