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Tris(trimethylsilyl)silane and Diphenylsilane in the Radical Chain Dideoxygenation of 1,6-Anhydro-D-glucose: A Comparative Study

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Abstract: The 2,4-bis-thionocarbonate 3 of 1,6-anhydro-D-glucose 1 can be transformed to the corresponding dideoxy compound 5 with diphenylsilane 7 as well as with tris(trimethylsilyl)silane 4 in a radical chain reaction.

Silanes are a group of hydrogen atom transfer agents[1] that can replace tributyltin hydride[2] and germanium hydrides[3] in radical chain reactions.[4] The silyl radical formed from the silanes by the initiator radical or other radicals in the chain is capable of carrying the radical chain.[5]

It has been shown recently, that tris(trimethylsilyl)silane,[6] phenylsilane,[7] diphenylsilane,[8] triphenylsilane,[8,9] tri-n-propylsilane,[10] triethylsilane,[11] 1,1,1,2,3,3,3-heptamethyltrisilane,[12] and tris(alkylthio)silanes,[13] as well as compounds containing a P-H bond[14] are all useful replacements of tin and germanium hydrides in radical chain chemistry.

Although the Si-H bond strength is very different in the various silanes studied,[15] it is possible to find conditions that allow the efficient use of any of these silanes as hydrogen atom transfer agents.

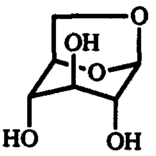
In a recent paper[16] the dideoxygenation of 1,6-anhydro-D-glucose was described with tributyltin hydride (60%), diphenylsilane (46%) and tris(trimethylsilyl)silane (86%). The reported reaction time was suspiciously long with diphenylsilane (10 h) and the yield was unreasonably low. These findings prompted us to study this 2,4-dideoxygenation reaction again and try either to explain or improve the reported data.

We are pleased to report herein that the reaction is indeed much better than it seemed in the light of the aforementioned publication. Thus, the commercially available 1,6-anhydro-D-glucose **1** (Aldrich) was treated with phenyl chlorothionoformate.[17] Although we have introduced[18,19] a series of other chlorothionoformates, **2b**, **2c**, **2d**, for the acylation and radical chain deoxygenation of alcohols and dideoxygenation of *vic*-diols, for comparison with the reported work[16] we repeated these experiments with the unsubstituted phenyl compound **2a**. The product of the acylation was the 2,4-*bis*-thionocarbonate 3 (m.p. 126-127°C, lit. 116-119°C; $[\alpha]_D^{25} = -51.7$ (c 1.2, $CHCl_3$) lit.[16] -50 (c 0.8, $CHCl_3$)).

Treatment of the *bis*-thionocarbonate 3 with tris(trimethylsilyl)silane 4 (2.2 equiv) and azobisisobutyronitrile (5 mol% relative to 3) in boiling toluene for 30 min afforded the known dideoxygenated product 2,4-dideoxy-1,6-

anhydro-D-glucose[20] **5**. The yield, determined by ^{1}H NMR was 87%, similar to the reported value (86%) ($[\alpha]^{28}_{D}$ = - 81.7° (c 1.2, H_2O), lit.[16] -80 (c 1, H_2O)).

This reaction was quenched in another run after 1 min to give a mixture of the two monodeoxy compounds **6a** and **6b** (57%) and the dideoxy compound **5** (38%). There was no sign of any cyclized intermediate as encountered in the dideoxygenation of 3,6-anhydro-D-pyranosides.[21]



1

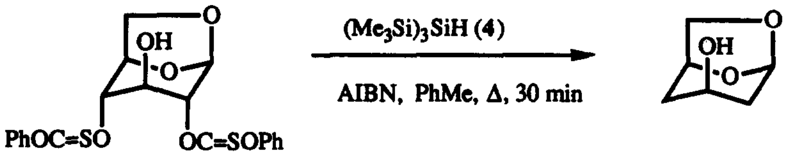
R—O-C(=S)-Cl

R = Ph **2a**

R = 2,4,6-tri-Cl-Ph **2b**

R = pentafluoro-Ph **2c**

R = 4-fluoro-Ph **2d**

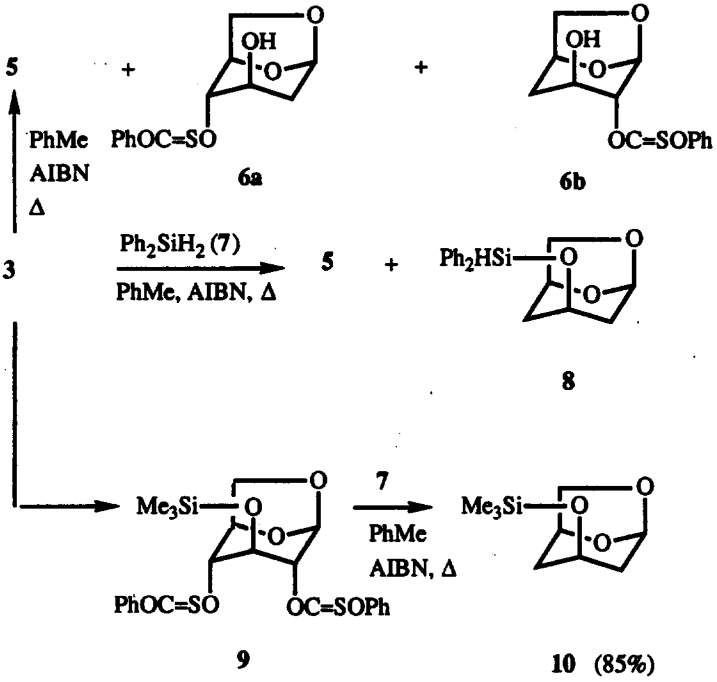


3

5 (87%)

The reaction of the *bis*-thionocarbonate 3 with diphenylsilane 7 (4 equiv) in boiling toluene, initiated by AIBN (1 equiv) gave 48% of 2,4-dideoxy-anhydro-D-glucose **5**, (reaction time 100 min) similarly to the reported yield (46%). However, the reaction mixture contained the two monodeoxy compounds **6a** and **6b** (28% isolated). The use of diphenylsilane as solvent (can be recovered) improved the yield of **5** only to 60%. The reaction with an increased amount of the radical initiator AIBN (1.4 equiv) in boiling toluene (140 min) furnished the dideoxy compound **5** in 60% yield. Tlc analysis of the reaction mixture showed the presence of a more mobile carbohydrate derivative. We assumed that this compound was a silylated derivative of 5. Treatment of the reaction mixture with 0.3 M aqueous potassium hydroxide solution removed this spot **8** and increased the yield of 5 by 14% to 74%. This yield was still not high, but this reaction showed to us that there was nothing wrong with the radical reaction with diphenylsilane 7. The product **5** was simply partly consumed in a silylation reaction of the type we observed recently with diphenylsilane.[22] This finding prompted us to test our conclusion. Earlier we used acetates and benzoates to protect hydroxyl groups and increase the yield of deoxygenations.[23] In this case we introduced a trimethylsilyl protecting group after the formation of the bis-thionocarbonate 3. This compound **9** was formed in the presence of triethylamine with chlorotrimethylsilane. The silylated intermediate **9** was not isolated but transformed directly to the silylated dideoxy compound **10**. Although there was no sign of any starting material or byproduct, the overall yield of the silylation and radical dideoxygenation steps was 85% (determined by ^{1}H NMR).

This compound, 1,6-anhydro-2,4-dideoxy-3-*O*-trimethylsilyl-D-glucose **10** (oil, $[\alpha]_D^{28}$ = - 70.0 (c 0.6, CH_2Cl_2), anal. calcd for $C_9H_{18}O_3Si$ C 53.46, H 8.91; found C 53.53, H 8.92%) was prepared also from the dideoxy compound **5** by silylation with trimethylsilyl chloride in the presence of triethylamine.



This finding indicates that with attention to details diphenylsilane **7** can give the same yield as tris(trimethylsilyl)silane **4** in radical chain deoxygenation reactions. This is further corroborated by the recent report of Buenger and Marquez.[24] They have dideoxygenated a *bis*-xanthate of a *vic*-diol with diphenylsilane in boiling toluene (initiated with AIBN) in 88% yield.

Typical procedure: The solution of 1,6-anhydro-2,4-*bis*-*O*-phenoxythiocarbonyl-D-glucose (0.1736 g, 0.4 mmol), chlorotrimethylsilane (0.304 ml, 2.4 mmol) and triethylamine (0.5 ml, 3.6 mmol) in benzene (3 ml) was stirred at r.t. for 1 h. After filtration the solvent was evaporated, the residue was dissolved in toluene and diphenylsilane (294 µl, 1.6 mmol) was added to the solution. The reaction mixture was then brought to the boil and treated under argon with 150 µL portions of AIBN solution (0.2624 g of AIBN in 3 mL of dioxane) 5 times (at every 20 min) during reflux. After evaporation of the solvent the residue was analyzed by NMR to give 85 % of the dideoxy product 1,6-anhydro-2,4-dideoxy-3-*O*-trimethylsilyl-D-glucose **10**.

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