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IMPROVED METHODS FOR THE RADICAL DEOXYGENATION OF SECONDARY ALCOHOLS*

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Summary. The reaction of Barton and McCombie has been improved by the use of the new reagents 2,4,6-trichlorophenoxythiocarbonyl chloride and its congener pentafluorophenoxythiocarbonyl chloride. Deoxygenations with these derivatives of 1,2:5,6-diacetoneglucofuranoside are fast and quantitative.

In the last decade there has been a marked increase in the use of radical reactions in Organic Synthesis.[1,2] The reason is simple. A panoply of reactions is now available which can give single products in high yield.

The radical deoxygenation of secondary alcohols, (Scheme 1) is one of the reactions of this kind.[3] It has been widely used for its original purpose[4] and, more recently, for the generation of radicals in carbohydrate chemistry.[5,6]

In the original publication[3] the group X was Ph, SMe and imidazolyl. Later Robins introduced[7] the group X variation PhO. The reagent PhO(CS)Cl is commercial and the derivatives are sometimes easier to make. It is also considered[6] to be more reactive. The MeO-derivative has also been employed.[8]

*This article is dedicated to Professor R. Bognár of Kossuth L. University, Debrecen, on the occasion of his 76th birthday.

Our experience with the radical chemistry of thiocarbonyl compounds led us to suspect that electron withdrawing groups in the X function would increase the radicophilicity of the thione group. At a suitable temperature this would increase the speed of the desired fragmentation and hence reduce the importance of side reactions.

We are pleased to report that when X is 2,4,6-trichlorophenoxy, or especially pentafluorophenoxy, the reaction with tributyltin hydride is rapid (minutes rather than hours) and the yields are excellent.

We have compared phenoxythiocarbonyl chloride[7] 1 with its 2,4,6-trichloro-analogue 2 and with the pentafluoro-reagent 3. We have also synthesized the pentachloro-reagent 4. All these derivatives were readily prepared from the appropriate phenol and thiophosgene.[9]

Acylations using 1 are normally catalyzed[7] by pyridine or by 4-dimethylaminopyridine (Steglich reagent).[10] We have obtained better results by using a catalytic (15-20%) amount of N-hydroxysuccinimide in benzene at 80° or in toluene at the same temperature with 1 equivalent of pyridine as HCl scavenger (5 hrs. for 2 with 5; 3 with 5 much faster). After completion of the acylation, a simple filtration removes the pyridine hydrochloride. The deoxygenation reaction can then be performed in the same solvent, which is a significant advantage over the previous procedure.

As a suitable model compound, we took 1,2:5,6-diactoneglucofuranoside 5. Previous studies[3,7,11] have given deoxygenation to 9 in high yield. The acylated derivatives 6, 7 and 8 were compared (Table 1). Without the initiator (AIBN) or the tributyltin hydride, there was no reaction. It is clear from this Table that 7 and 8 are reduced faster than 6 and that quantitative yields of 9 are formed in a short period of time. We have also isolated crystalline 7 (m.p. 90-92°C) and 8 (m.p. 66-67°C) and have shown that they are quantitatively reduced to 9.

We have also examined the pentachloro-derivative 10. This is also smoothly deoxygenated but it gives by-products during the acylation step, which are not derived from 5. This complicates the work-up.

Competition experiments between 6 and 7 and between 6 and 8 are summarized in Table 2. The new reagent systems 7 and 8 clearly react significantly faster than reagent system 6.

Table 1[a]

Entry	Bu_3SnH (eq.)	Temp °C (bath)	Time (mins)	9%		
				6	7	8
1	1.5	100	3	45	64	90
2	1.5	110	3	65[b]	75	90
3	2.0	110	5	--	100	--
4	1.5	110	15	72	100	--
5	1.5	110	5	66[b]	--	100

a. The reactions were carried out under argon in 0.02M C_6D_6 solutions in sealed NMR tubes. AIBN (0.5 mg/ml) was used in each experiment. After the reaction times indicated, the reaction mixtures were cooled in ice and 200 MHz ^1H NMR spectra measured at ambient temperature with an internal reference.

b. By-products were formed.

Table 2[a]

Bu_3SnH[b] (eq.)	Time (min)	Temp. (°C)	% measured		
			7	6	9[d]
0.25[b]	0	80	100	100	0
0.5[b]	30	80	80	100	20
0.75[b]	60	80	30	100	58
	90	80	9	70	122
			% measured		
			8	6	9[d]
1.5[c]	3	100	10	70	120

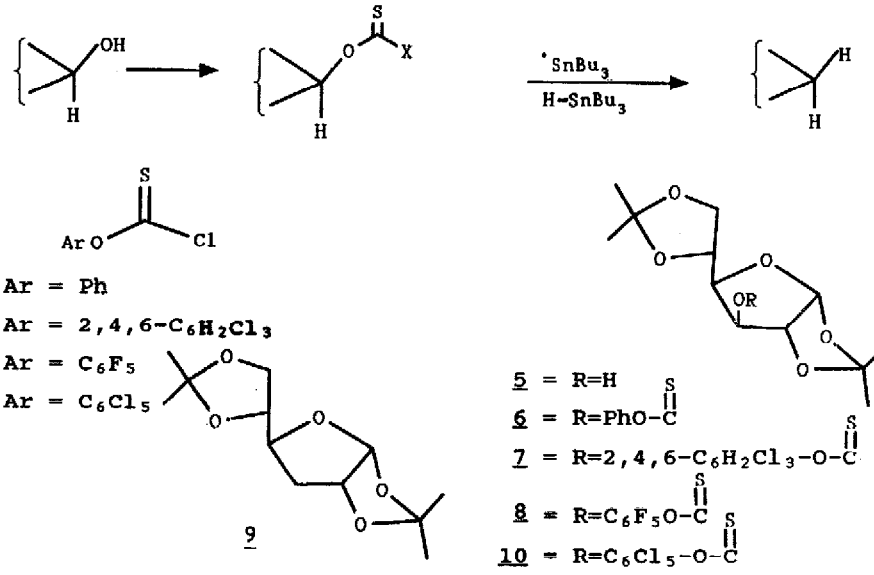
a. AIBN was used as a radical initiator.

b. The reaction was carried out under dry argon in boiling benzene in a 90°C oil bath. Samples were taken from the reaction mixture before the addition of the next 0.25 equivalent of Bu_3SnH, evaporated and the amounts determined by 200MHz ^1H NMR in $CDCl_3$ solution (TMS, ref.).

c. This reaction was carried out in C_6D_6 solution in a sealed NMR tube under argon. The yield of 9 is based on formation of 2 mols.

d. Observed yield of 9; theory 200% maximum.

Scheme 1



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