Free Radical Substitutions of Acyloxy Groups in Carbohydrate α-Ketoesters

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A range of carbohydrate derivatives containing α-ketoester functionality undergo efficient reductive loss of the acyloxy groups when treated with tri-n-butyltin hydride in refluxing benzene and in the presence of azoisobutyronitrile (AIBN) as radical initiator; under similar conditions, but with allyltri-n-butyltin instead of the hydride, efficient α-*C*-allylation takes place with axial substitution occurring preferentially in compounds with the ketoesters located within conformationally stable pyranoid rings; the methods represent novel ways of deoxygenating carbohydrate derivatives and of introducing branch points.

The 'tin method'[1] offers a simple means of generating organic free radicals that are of immense value in modern synthetic procedures.[2] In carbohydrate chemistry, compounds containing carbon–halogen or carbon–mercury bonds, thionocarbonate esters of various kinds, nitro-compounds, isocyanides and phenylthio- and phenylseleno-derivatives are frequently used as radical sources, and in derivatives that do not permit more elaborate processes (for example radical cyclisations) tri-n-butyltin hydride, in the presence of AIBN as initiator, causes reductive removal of the functional groups. With allyltri-n-butyltin, instead of the hydride, the intermediate carbon radicals abstract allyl groups from the reagent with the consequential replacement of the functional groups by *C*-bonded allyl groups, and this latter reaction can be used to elaborate the carbon skeletons of the carbohydrate moieties.[3]

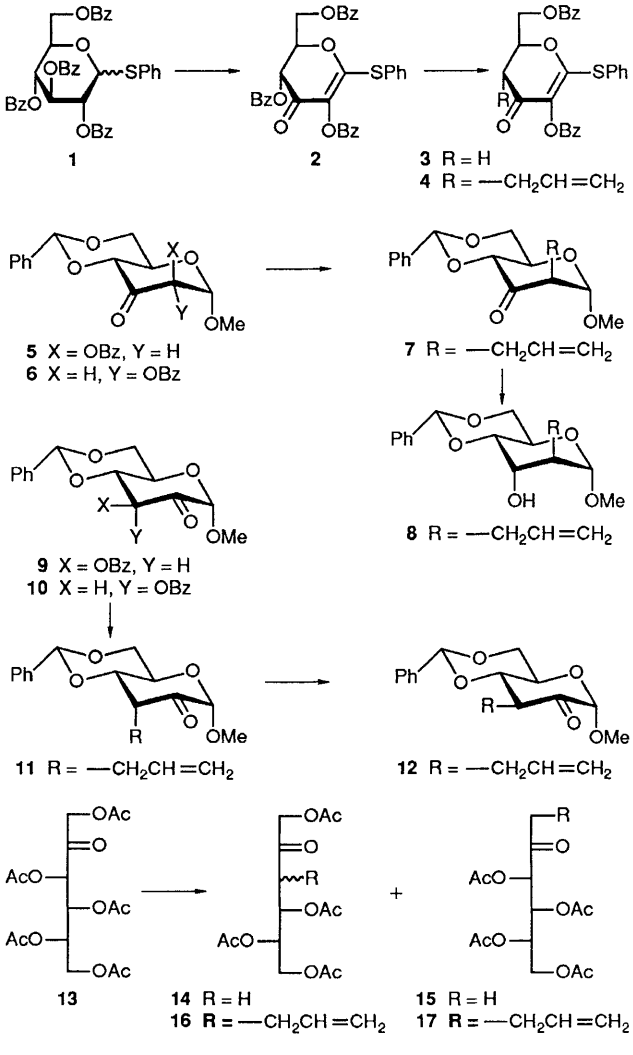
We report that α-keto acyl esters also serve as sources of free radicals when treated with these reagents, and thereby provide a means of allowing specific deoxygenations and carbon–carbon bond forming processes. While branched-chain sugar derivatives having a *C*-bonded acyl group and a benzoyloxy group at the same carbon centre have previously been shown to undergo reductive loss of the benzoyloxy group on treatment with tri-n-butyltin hydride and AIBN,[4] we are not aware that the more general value of α-ketoesters in free radical chemistry has been recognised.

Treatment of the highly functionalised α-ketoester **2**, which is obtainable directly and in high yield by radical photobromination of *S*-phenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-α- or β-D-glucopyranoside **1**,[5] in refluxing benzene with the hydride and catalytic amounts of AIBN gave the 4-deoxy product **3** {72% after chromatography, $[\alpha]_D^{25}$ +239° (CH_2Cl_2)}. With allyltri-n-butyltin the 4-*C*-allyl product **4** was obtained (80%, m.p. 123–125 °C, $[\alpha]_D^{25}$ +157° (CH_2Cl_2), $J_{4,5}$ 10.1 Hz).

Applied separately to the D-*arabino*- and D-*ribo*-3-ulosides **5**, **6**, respectively, the allylation procedure afforded almost quantitative yields of the 2-*C*-allyl-2-deoxy-D-*arabino*-derivative {**7**, m.p. 91–93 °C, $[\alpha]_D^{25}$ +33° ($CHCl_3$), $J_{1,2}$ 0 Hz}. Reduction of **7** with lithium aluminium hydride gave the alcohol **8** {29% isolated, major product, m.p. 105–107 °C, $[\alpha]_D^{25}$ +73° ($CHCl_3$)} the low magnitude of the $J_{1,2}$ and $J_{2,3}$ values of which (both <1 Hz; $J_{3,4}$ 2.3, $J_{4,5}$ 9.7 Hz) allowed the assignment of the D-*altro*-configuration.[6] Both epimers **5** and **6** gave the same product of allylation, which suggests that they react by a common intermediate as has been observed previously in related radical substitution reactions at epimeric centres of isomers.[4,7]

In the cases of the 2-uloside epimers **9** and **10** both, again, gave the same product **11** {87%, $[\alpha]_D^{25}$ +57° (CH_2Cl_2), $J_{3,4}$ 5.8, $J_{4,5}$ 9.4 Hz}, but this C-3 axial epimer isomerised readily on leaving to stand in diethyl ether over silica gel or in diethyl ether or ethanol over Amberlite IR 120 (H^+) ion exchange resin to give the thermodynamically preferred *arabino*-product **12** {m.p. 100–102 °C, $[\alpha]_D^{25}$ +59° (CH_2Cl_2), $J_{3,4}$, $J_{4,5}$ 10.3 Hz} devoid of diaxial interactions between the substituents at C-1 and C-3. Compound **7** could not be induced to isomerise, and its epimer was not detected at any stage in the reaction of the precursors **5** and **6**. It is concluded that the α-keto radicals derived from compounds **5**, **6**, **9** and **10** react under kinetic control to give products with the allyl groups in the axial orientation. The radical derived from the 2-ulosides **9** and **10** initially affords compounds **11**, which is evidence that a stereoelectronic effect akin to that operating at the anomeric centre of aldopyranosyl radicals[8] controls the reaction. Steric factors would have led to the formation of the D-*arabino*-epimer.[8]

L-Sorbose 1,3,4,5,6-pentaacetate **13** allowed us to investigate a ketone with two distinguishable α-ester groups. On treatment with tri-n-butyltin hydride and AIBN it gave two chromatographically distinguishable products, the major product being the 3-deoxy compound **14**, the other being an inseparable mixture of 1-deoxy compounds including **15** and



Scheme 1

3,4-dideoxy-3-enes. Radical allylation of compound **13** gave the 3-*C*-allyl product **16** {$[\alpha]_D^{25}$ −22° (CH_2Cl_2), 4 : 3 mixture of epimers} and the 1-*C*-allyl isomer **17** {$[\alpha]_D^{25}$ −1° (CH_2Cl_2)} in a ratio of 2 : 1.

New compounds were characterised by ^1H and ^{13}C NMR spectroscopic methods and gave satisfactory elemental analyses. The relationships between the compounds described are shown in Scheme 1.

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