

## Free Radical Substitutions of Acyloxy Groups in Carbohydrate $\alpha$ -Ketoesters

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A range of carbohydrate derivatives containing  $\alpha$ -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  $\alpha$ -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'<sup>1</sup> offers a simple means of generating organic free radicals that are of immense value in modern synthetic procedures.<sup>2</sup> 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.<sup>3</sup>

We report that  $\alpha$ -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 benzyloxy group at the same carbon centre have previously been shown to undergo reductive loss of the benzyloxy group on treatment with tri-*n*-butyltin hydride and AIBN,<sup>4</sup> we are not aware that the more general value of  $\alpha$ -ketoesters in free radical chemistry has been recognised.

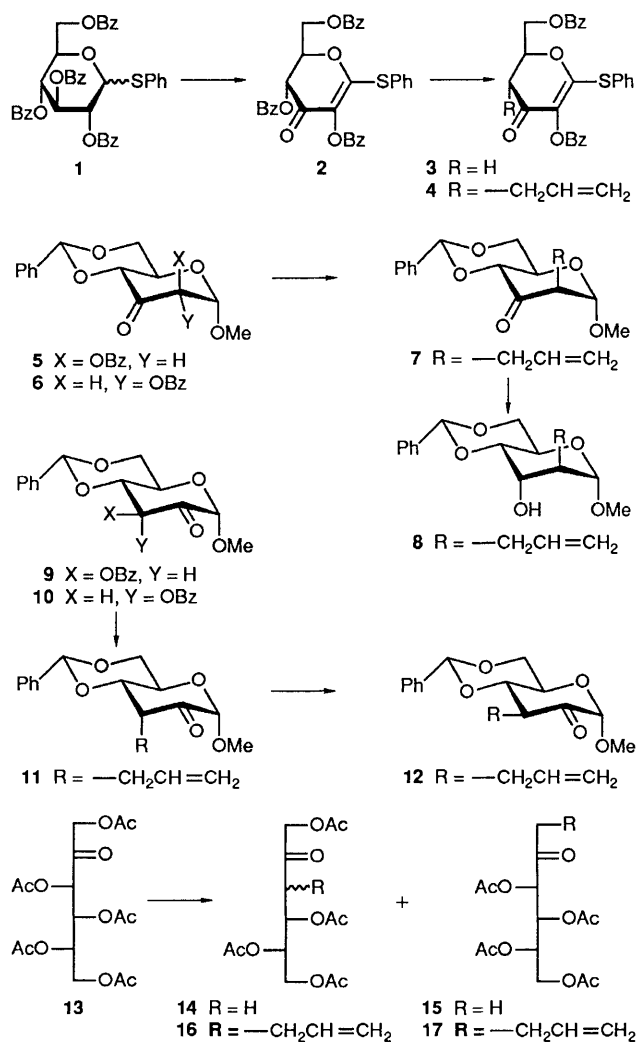
Treatment of the highly functionalised  $\alpha$ -ketoester **2**, which is obtainable directly and in high yield by radical photobromination of *S*-phenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio- $\alpha$ - or  $\beta$ -D-glucopyranoside **1**,<sup>5</sup> in refluxing benzene with the hydride and catalytic amounts of AIBN gave the 4-deoxy product **3** (72% after chromatography,  $[\alpha]_D^{25} +239^\circ$  (CH<sub>2</sub>Cl<sub>2</sub>)). With allyltri-*n*-butyltin the 4-C-allyl product **4** was obtained (80%, m.p. 123–125 °C,  $[\alpha]_D^{25} +157^\circ$  (CH<sub>2</sub>Cl<sub>2</sub>),  $J_{4,5}$  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,  $[\alpha]_D^{25} +33^\circ$  (CHCl<sub>3</sub>),  $J_{1,2}$  0 Hz). Reduction of **7** with lithium aluminium hydride gave the alcohol **8** (29% isolated, major product, m.p. 105–107 °C,  $[\alpha]_D^{25} +73^\circ$  (CHCl<sub>3</sub>)) 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.<sup>6</sup> 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.<sup>4,7</sup>

In the cases of the 2-uloside epimers **9** and **10** both, again, gave the same product **11** (87%,  $[\alpha]_D^{25} +57^\circ$  (CH<sub>2</sub>Cl<sub>2</sub>),  $J_{3,4}$  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<sup>+</sup>) ion exchange resin to give the thermodynamically preferred *arabino*-product **12** {m.p. 100–102 °C,  $[\alpha]_D^{25} +59^\circ$  (CH<sub>2</sub>Cl<sub>2</sub>),  $J_{3,4}$ ,  $J_{4,5}$  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

$\alpha$ -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<sup>8</sup> controls the reaction. Steric factors would have led to the formation of the D-*arabino*-epimer.<sup>8</sup>

L-Sorbose 1,3,4,5,6-pentaacetate **13** allowed us to investigate a ketone with two distinguishable  $\alpha$ -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**  $\{[\alpha]_D^{25} -22^\circ (\text{CH}_2\text{Cl}_2)$ , 4:3 mixture of epimers} and the 1-*C*-allyl isomer **17**  $\{[\alpha]_D^{25} -1^\circ (\text{CH}_2\text{Cl}_2)\}$  in a ratio of 2:1.

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

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## References

- 1 B. Giese, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 553.
- 2 W. P. Neumann, *Synthesis*, 1987, 665; M. Ramaiah, *Tetrahedron*, 1987, **43**, 3541; D. P. Curran, *Synthesis*, 1988, **417**, 489.
- 3 G. E. Keck, E. J. Enholm, J. B. Yates and M. R. Wiley, *Tetrahedron*, 1985, **41**, 4079; C. K. Chu, B. Doboszewski, W. Schmidt and G. V. Ullas, *J. Org. Chem.*, 1989, **54**, 2767.
- 4 H. Redlich, H.-J. Neumann and H. Paulsen, *Chem. Ber.*, 1977, **110**, 2911.
- 5 R. J. Ferrier and R. H. Furneaux, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1993.
- 6 G. Kotowycz and R. U. Lemieux, *Chem. Rev.*, 1973, **73**, 669.
- 7 R. Blatner and R. J. Ferrier, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1523.
- 8 B. Giese, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 969.