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The Quasi-Homo-Anomeric Interaction in Substituted Tetrahydropyranyl Radicals: Structure and Kinetics of Formation

Athelstan L.J. Beckwith[a] and Peter J. Duggan *[b]

[a]Research School of Chemistry, Australian National University, Canberra, 0200, Australia

[b]Department of Chemistry, Monash University, Clayton, Melbourne, Victoria, 3168, Australia

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Abstract: The EPR spectra of 3-acyloxytetrahydropyran-2-yl radicals (**8** and **9**) indicate that these species preferentially adopt conformations in which the orientation of the ester group allows maximum overlap between the SOMO, the lone pair on the ring oxygen, and the σ* orbital of the C-O bond. These observations support earlier proposals that the same type of stabilising interaction affects the conformations of more complex glycosyl radicals. The rates of formation of **7** and **8** from the corresponding aryl sulfides are affected by this "quasi-homo-anomeric" interaction. © 1998 Elsevier Science Ltd. All rights reserved.

Following early studies on the radical chemistry of tetrahydropyranyl systems,[1,2,3] it has become widely accepted that the conformations of carbon-centred radicals bearing an α-oxygen substituent often reflect a stabilising interaction between the SOMO orbital and the adjacent HOMO of the oxygen lone pair.[4] The same interaction also affects the stereoselectivity of their formation and reactions. This interaction is sometimes loosely referred to as an anomeric effect although it involves overlap of the lone pair with a semi-occupied p-orbital rather than a vacant σ* orbital.[5,6,7] In six-membered rings it stabilises transition structures for the formation or fission of axial bonds by comparison with those for equatorial bonds. Consequently, conformationally locked tetrahydropyran-2-yl radicals often react in a highly diastereoselective fashion to give axially substituted products.[8,9] Such reactions can be synthetically useful.

More recently, Barton proposed another type of pseudo anomeric effect involving a stabilising interaction between the SOMO of a carbon-centred radical and the vacant σ* orbital of a β-C–O bond.[10,11,12] Since such an interaction should be maximised when the SOMO and the C–O bond are coplanar, carbon centred radicals containing a β-oxygen substituent which can assume this preferred conformation should be generated more readily than comparable unsubstituted radicals. Also, they should exhibit restricted rotation and should react diastereoselectivity. Although some reactions of suitably substituted substrates appear to support these hypotheses,[13,14,15,16] firm quantitative evidence for the existence of this type of 'β-oxygen effect' has not yet been forthcoming.[17]

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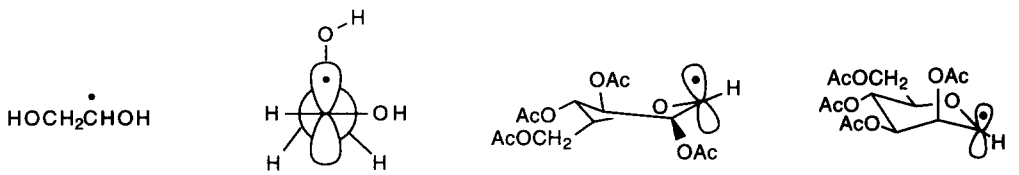
A combination of both these effects, "quasi-homo-anomeric" stabilisation, has been invoked by Giese and Sustmann to rationalise their observations on the chemistry of a variety of carbohydrate radicals.[18,19] Their suggestion that a stabilising interaction can occur when a radical centre is flanked by an oxygen lone pair and a β-C–O bond, and that the overlap will be maximised when the SOMO, an orbital containing an oxygen lone pair, and the σ^* of the C-O bond are coplanar, is consistent with EPR determined conformations of simple acyclic radicals and of complex cyclic species. For example the dihydroxyethyl radical **1** preferentially adopts the conformation **2** consistent with this hypothesis and exhibits a significant barrier to rotation.[20] Evidence for a similar effect in tetrahydropyran-2-yl radicals substituted in the 3-position by hydroxy[21] and fluoro[22] groups has also been found. Likewise, Giese, Sustmann and Korth have presented EPR evidence indicating that C-1 sugar radicals substituted with electronegative groups at C-2 and electron acceptors or hydrogen at C-1, attempt to adopt a conformation that maximises orbital interactions between the HOMO of the ring oxygen, the SOMO and the σ^* orbital of the β-C-O bond. The stabilisation that results from such an interaction is apparently able to counteract all but the most severe of competing steric effects. For example the tetraacetoxy glucopyranos-1-yl radical adopts the $B_{2,5}$ conformation **3** whereas the tetraacetoxy mannopyranos-1-yl radical can achieve the proposed interaction in the $^4C_1$chair conformation **4**.[18,19]



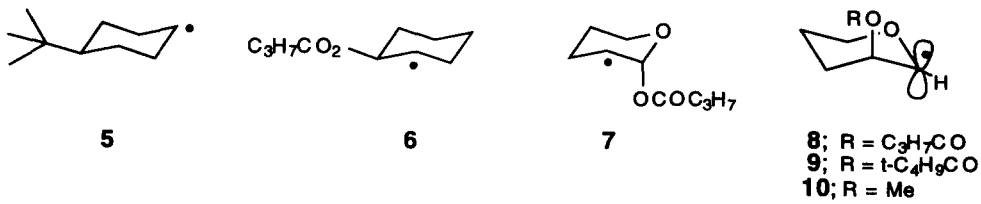
1 **2** **3** **4**

Figure 1

When attempting to rationalise the conformations of radicals such as **3** and **4**, it is difficult to discern the influence of the several substituents not involved in the "quasi-homo-anomeric" interaction. We have, therefore, examined the structure of a number of more simple cyclic radicals unencumbered by superfluous substituents and have obtained results consistent with the proposed stabilising effect.

Results and Discussion

EPR Spectra. The EPR spectral data for a variety of cyclic radicals are given in Table 1. In each case the radicals were generated by continuous UV irradiation of a cyclopropane solution of di-t-butyl peroxide, triethylsilane, and an appropriate bromide or chloride (**23** - **27**, see Fig 6).[20] Hyperfine splitting constants (hfc's) were determined by a least squares fit between experimental and simulated spectra.[23] The spectrum of the 4-t-butylcyclohexyl radical **5** in which the substituent is pseudo equatorial was recorded for reference. As expected[24] it showed a large triplet hfc of 41.93G assigned to the two pseudo-axial β-protons, and a relatively small triplet (hfc = 6.37G) assigned to the two pseudo-equatorial β-protons. The α-proton hfc (21.06G) was very similar to those for the radicals **3** and **4**. In each case the value is consistent with a radical localised on an essentially planar carbon centre.



5 **6** **7** **8**; R = C_3H_7CO **9**; R = t-C_4H_9CO **10**; R = Me

Figure 2

The 2-butanoyloxycyclohexyl radical **6** has EPR data characteristic of an equatorially substituted chair-like species. The spectrum shows only one small doublet splitting (hfc = 5.87G) consistent with a single pseudo-equatorial β-proton, but the presence of two pseudo-axial β-protons at the 2- and 6-positions is indicated by the two large doublet hfc's (41.68 and 36.42G). Although these two splittings cannot be assigned individually to the β-protons, molecular mechanics calculations suggest that the larger value arises from the proton at C-6. These results clearly indicate that the radical **6** has the conformation shown with the butanoyloxy substituent in an equatorial position. If there is a β-oxygen effect, it is insufficient to hold the ester substituent in the pseudo-axial orientation required for the most effective overlap of the SOMO with the adjacent σ^* LUMO.

Table 1. EPR Data for Substituted Cyclic Radicals.

Radical[a]	Temp.(K)	Hyperfine splitting constants (G)[b]			
		α	β	γ[c]	δ[c]
5	200	21.06 (1)	41.93 (2)	1.07 (2)	
			6.37 (2)	0.64 (2)	
6	180	20.61 (1)	41.68 (1)	2.81 (1)	
			36.42 (1)	1.12 (1)	
			5.87 (1)		
7	180	21.82 (1)	48.42 (1)	9.06 (1)	0.74 (2)
			13.28 (2)[d]	0.35 (1)	
8	240	17.80 (1)	6.12 (1)	3.77 (1)	0.60 (2)
9	240	17.77 (1)	5.84 (1)	3.75 (1)	0.61 (2)

Footnotes: a; All radicals had g factors between 2.0023 and 2.0029. b; The number of equivalent nuclei causing splitting, as indicated by the spectral analyses, are in parentheses. c; All γ and δ hyperfine splitting assignments are tentative. d; Presumably an exchange averaged splitting.

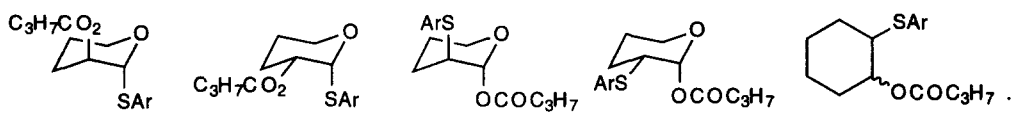
On the other hand the EPR data for the radical **7** suggest that, where the classical anomeric effect is possible, the ester substituent takes up the expected pseudo-axial orientation. This is consistent with the relatively small triplet (hfc 13.28G) assigned to two pseudo-equatorial β-protons, but only one large doublet (hfc 48.21G) attributable to a single pseudo-axial β-proton.

The EPR spectrum of the 3-butanoyloxytetrahydropyranyl-2-yl radical **8** shows very different characteristics from its cyclohexyl analogue **6**. In this case the small value of the β-proton hfc (6.12G) indicates that the sole β-C-H bond is essentially orthogonal to the SOMO, i.e. it is pseudo-equatorial and

the ester group must therefore be pseudo-axial. The EPR data for the pivaloyloxy substituted radical **9** lead to the same conclusion. Despite the large steric bulk of the substituent, the low value of the β-proton hfc (5.84 G) indicates that the ester group still remains axial. These observations are consistent with the view that a stabilising "quasi-homo-anomeric" interaction between the σ^* LUMO, the SOMO and the lone pair HOMO in **8** and in **9** is sufficient to lock the ester substituents in the pseudo-axial orientation. They are in full agreement with the previous EPR studies of carbohydrate radicals and suitably substituted acyclic species, and with the results of semi-empirical calculations which show that the related axially methoxy substituted radical **10** is stabilised relative to its equatorial conformer.[25]

It is not immediately clear from the EPR data whether the radicals **8** and **9** preferentially assume twist boat or chair forms. However, the close similarity of the EPR data to those for the mannopyranosyl radical **4** strongly indicates that **8** and **9** are in the chair form as shown. Support for this conclusion comes from molecular calculations which show that the twist boat forms of **8** and **9** have strain energies higher than those of the chair forms.

Kinetics of Homolytic Attack on S-C Bonds. It has been proposed that the "quasi-homo-anomeric" interaction can also influence the rate of formation of certain radicals. While carrying out an earlier study of the β-acyloxyalkyl radical rearrangement[26] we found that the diastereoisomers **11** and **12** had different rates of reaction with tributyltin hydride. In an attempt to rationalise this observation we have now compared the analogous stannane reactions of **11** and **12**, and the diastereoisomers **13** and **14**, with those of the two substituted cyclohexane diastereoisomers **15** and **16** (Table 2).



11 **12** **13** **14** **15**, cis- **16**, trans-

(Ar = *p*-tolyl)

Figure 3

The exact stereochemistry of each substrate, which was of prime importance in deducing the cause of the unexpected kinetic behaviour, was determined through the use of standard NMR techniques. In the case of the 2-sulphide the assignment could not be made simply by comparison of the ^{1}H NMR spectra of **11** and **12**, as in this case the coupling constants between H-2 and H-3 ($J_{2,3}$), which are usually very indicative of substituent patterns of this type,[27] are virtually identical (4 Hz). This is not so in the case of the parent *trans* alcohol[26] for which $J_{2,3}$ (7.1 Hz) for the *trans* isomer is larger than that (3.8 Hz) of the *cis*. When a mixture of the *cis* and *trans* isomers of the alcohol containing a predominance of the former was esterified in high yield with butyryl chloride in pyridine/ether, the major product was assumed to be the *cis* isomer **12** of the ester. This allowed the NMR spectra of the two isomers to be identified. The $J_{2,3}$ coupling for the minor *trans*- product (4Hz) is too small for H-2 and H-3 to be diaxially disposed.[27] Hence the substituents at C-2 and C-3 must be diaxial as shown in **11**. This probably reflects the S-C-O anomeric

effect, which, although weaker than its O-C-O analogue,[28] must be sufficient to outweigh the opposing 2,3-diaxial interactions.

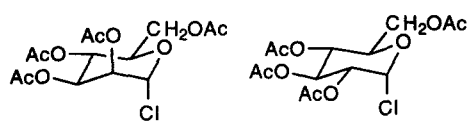
In the case of the 3-sulphide, the stereoisomers **13** and **14** were distinguished by their $J_{2,3}$ coupling constants (*trans* 5.4 Hz, *cis* 3.2 Hz). The magnitude of the coupling for the *trans* stereoisomer **13** implies that the substituents are also diaxially oriented. This is reasonable in view of the strong O-C-O anomeric effect.

Of the cyclohexane species (**15** and **16**) the substituents of the *trans* isomer (**16**) were assumed to be diequatorially disposed, since here there is no possibility of electronic effects overriding the steric factors involved. Axial protons usually resonate upfield of equatorial protons in the ^{1}H NMR spectra of cyclohexanes,[27] and on this basis the isomer with the higher field resonances for H-1 and H-2 was assigned as *trans*. In support of this conclusion, the coupling patterns of H-1 and H-2 in the spectrum of **16** are very similar, as expected for protons with similar orientations.

Table 2. Relative Rates of Reaction of $Bu_3Sn^\bullet$ with Diastereomeric Pairs of Substrates in Benzene at 80°C

Substrates	Relative reactivity
11 : **12**	2.9 : 1.0
13 : **14**	2.5 : 1.0
15 : **16**	1.1 : 1.0
17 : **18**	7.8 : 1.0[a]

Footnote: a; Data taken from ref 18.



17 **18**

Figure 4

The differences between the reaction rates of pairs of diastereomers with tributyltin hydride were quantified by competition experiments. In each case a solution (~ 0.05 M) in benzene of a mixture of the two diastereoisomers in known proportions was allowed to react at 80°C with ~0.55 equivalents of tributyltin hydride in the presence of AIBN. After the stannane had been consumed, the relative amount of each isomer remaining was measured, either by GC with biphenyl as an internal standard, or by ^{1}H NMR spectroscopy. The relative rates of reaction were then obtained by substitution of the data into eqn 1.[29]

$$k_{trans}/k_{cis} = \{\log[trans]_f - \log[trans]_0\}/\{\log[cis]_f - \log[cis]_0\} \quad (1)$$

A brief examination of the results of the competition reactions (Table 2) reveals that in the case of the pyrans the *trans* diaxial isomers **11** and **13** are significantly more reactive than the corresponding *cis* axial-

equatorial isomers **12** and **14**, yet the isomers **15** and **16** of the cyclohexyl compound have essentially equivalent reactivity towards stannyl radicals. In a similar study, it was found that axial cyclohexyl bromides react with stannane faster than the corresponding equatorial isomers.[30] It was suggested that the difference in rates reflected the difference in ground state energies; the axial compound being higher in energy than the equatorial. If the transition structures for both isomers were of similar energy, the reaction of the axial isomer would then have the lower activation energy. This explanation is unlikely to apply to the present situation, however, since the *trans* diaxial compound **11** is expected to be lower in energy than its *cis* isomer **12**. This is supported by molecular modeling calculations[6] on the related acetate which indicated that the *trans* diaxial isomer **19** is lower in energy than the *cis* isomer **20**. Calculations performed on the compound with reverse regiochemistry indicated that its *trans* diaxial isomer **21** and the *cis* isomer **22** are of similar energy.

19 **20** **21** **22**

Figure 5

A more plausible explanation for the variation of reactivity between these stereoisomers is that it reflects the relative orientation of the ester and the sulphide. When the dihedral angle between the C-S bond and the β-C-O bond (θ) is close to 0° or 180° "quasi-homo-anomeric" stabilisation can affect the energy of the transition structure for C-S bond homolysis. This is the case for the *trans* diaxially substituted pyrans where $\theta \approx 180°$. However, for the *cis* isomers where $\theta \approx 60°$, deformation of the ring must occur before maximum overlap between the relevant orbitals can take place. The fact that the *trans* isomer reacts more rapidly with stannane than the *cis* isomer, even though its ground state energy is expected to be somewhat lower indicates that "quasi-homo-anomeric" stabilisation has a significant affect on transition structure energy. This is somewhat analogous to the so called anomeric effect that favours the abstraction of axial hydrogens adjacent to the oxygen atom in tetrahydrofurans and similar heterocycles.[1,2] As expected, there is no such preferential reaction of the *trans* cyclohexane isomer **16** in which the "quasi-homo-anomeric" effect cannot operate. Indeed the *cis* isomer **15** is slightly more reactive than the *trans*, presumably because it has the higher ground state energy. These results are similar to those reported by Giese and co-workers[18] who showed that the mannosyl chloride **17** reacts faster with stannane than the glucosyl chloride **18**. In that case the difference in reactivity is quite pronounced possibly because the rigid nature of these substrates holds the acetate at C-2 in **17** in the axial orientation much more rigorously than is the case for the butyrate substituent in the tetrahydropyran **11**.

Finally, it is interesting to note that the order of the substituents does not appear to have a significant affect on the apparent bond weakening process in the tetrahydropyranyl radicals, as is shown by the similarity in rate enhancement for the *trans* isomers of both **11** and **13**. This probably reflects the difference in ground state energies of the two isomers, but it might also indicate that a type of homo anomeric stabilising interaction can occur when a C-O bond is flanked by an oxygen lone pair and a SOMO on carbon.

Conclusions

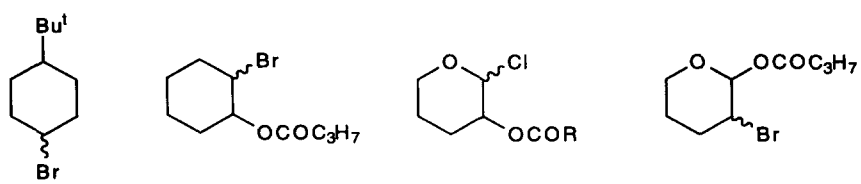
The EPR studies described above indicate the that 3-acyloxytetrahydropyran-2-yl radicals **8** and **9** preferentially adopt conformations that allow maximisation of the overlap between the SOMO, the orbital containing the ring oxygen lone pair and the σ* of the β-C-O bond. These observations strongly support the existence of the "quasi-homo-anomeric" effect, a stabilising interaction that operates when a carbon centred radical is flanked by an oxygen atom and a C-O bond. This effect was initially invoked to explain the conformations and reactions of highly substituted pyranose radicals. The results of the current study provide evidence for the same stabilising interaction in much less complicated 3-acyloxytetrahydropran-2-yl radicals and thus show that the earlier results were not induced by the many extraneous substituents.

The "quasi-homo-anomeric" effect is also apparently reflected in the kinetics of the formation of **8** from aryl sulfides. Furthermore the relative rates of reaction of **13** and **14** with $Bu_3Sn^{\bullet}$ suggest that a similar stabilising interaction may operate when a C-O bond is flanked by an oxygen lone pair and a SOMO on carbon.

Diastereoselective reactions of 3-acyloxytetrahydropyran-2-yl radicals with alkyltin reagents will be described in a forthcoming publication.

Experimental

General. ^1H and ^{13}C NMR spectra were recorded as $CDCl_3$ solutions on either a VARIAN XL-200 spectrometer (200 MHz for ^1H) or a VARIAN VXR-300 spectrometer (300 MHz for ^1H) and are reported in parts per million downfield from the tetramethylsilane internal reference (δ). Low resolution mass spectra were recorded on a VG MICROMASS 7070 F mass spectrometer operating at 70 eV for electron impact ion generation (EI) or using ammonia for chemical ionisation (CI). High resolution mass spectra were obtained on an AEI MS 902 high resolution mass spectrometer. EPR spectra were recorded on a BRUKER 200D-SRC spectrometer. Radicals were generated by continuous UV irradiation of a cyclopropane solution of di-t-butyl peroxide, triethylsilane, and the appropriate bromide or chloride (**23**[31] - **27**). Before a spectrum was recorded, the samples were deoxygenated by the passage of a slow stream of N_2, and were kept under an atmosphere of N_2 while spectra were recorded. Values of *g* were determined absolutely, using a BRUKER ER 035 NMR gaussmeter and a HEWLETT-PACKARD 5245L frequency counter equipped with 5257A transfer oscillator. The spectrometer was equipped with a BRUKER ER 4111 variable temperature unit and an irradiation system which used a HANOVIA L5173 Hg (Xe) lamp. A more detailed description of the instrumentation employed has been described previously by Brumby and Beckwith.[23] The arylsulfides **11- 14** were prepared as described previously.[26]



23 **24** **25; R = C_3H_7** **26; R = t-C_4H_9** **27**

Figure 6

trans-*1-Butanoyloxy-2-bromocyclohexane* (trans-*24*). The title compound was prepared by the treatment of the corresponding bromo-hydrin[32] (1.0 g, 5.6 mmol) with butyryl chloride and pyridine in dry diethyl ether according to the standard method.[26] It was isolated as a slightly brown coloured oil (1.1 g, 79%) by means of vacuum liquid chromatography.[33] ^{1}H NMR (200 MHz) δ 0.90-2.50 (m, 15H, -COC*H*$_2$C*H*$_2$C*H*$_3$, H$_2$-3, 4, 5, 6), 3.96 (d of t, 1H, $J_{2,3}$ = 5, $J_{1,2}$ = 13Hz, H-2), 4.80-4.96 (m, 1H, H-1); ^{13}C NMR (75 MHz) δ 13.25 (-CH$_2$*C*H$_3$), 18.1 (-*C*H$_2$CH$_3$), 23.0 (C-4), 25.2 (C-5), 30.9 (C-3), 35.4 (C-6), 36.0 (-*C*OCH$_2$-), 52.6 (C-2), 75.3 (C-1), 172.7 (C=O); IR (film) 1740 (C=O), 695 (C-Br) cm^{-1}; MS (EI) *m/z* 169 (weak), 162 (3%), 160 (3), 81 (57), 71 (100); Anal. Calcd for $C_{10}H_{17}BrO_2$: C, 48.21; H, 6.88. Found: C, 48.18; H, 7.00.

2,3-Dibutanoyloxytetrahydropyran. Treatment of tetrahydropyran-2,3-diol[26] (1.35 g, 11 mmol) with butyryl chloride (1.3 mL, 12 mmol) and pyridine (1.0 mL, 12 mmol) under the conditions previously described for preparation of **11/12**,[26] afforded the desired diester as a brown oil. It was purified by means of flash chromatography (ethyl acetate / hexane) to yield the desired diester as a colourless oil (1.33 g, 50%). A sample was distilled at 63°C and 0.4 mm Hg (Kugelrohr). ^{1}H NMR (200 MHz) δ 0.90-1.10 (m, 6H, -CH$_2$C*H*$_3$), 1.60-2.45 (m, 12H, -COC*H*$_2$C*H*$_2$-, H$_2$-4, 5), 3.60-4.00 (m, 2H, H$_2$-6), 4.70-4.80 (m, 0.66H, H-3 *trans*), 4.88-5.02 (m, 0.34H, H-3 *cis*), 5.83 (d, 0.66H, J = 3.7Hz, H-2 *trans*), 6.14 (d, 0.34H, J = 3.2Hz, H-2 *cis*); ^{13}C NMR (50 MHz) δ 13.5 (-CH$_2$*C*H$_3$), 18.1, 18.2, 18.3, 18.3 (-*C*H$_2$CH$_3$), 20.8, 23.5, 23.7, 24.4 (C-4, 5), 35.9, 36.0, 36.1, 36.2 (-*C*OCH$_2$-), 61.3, 62.8 (C-6), 67.4, 68.3 (C-3), 89.7, 91.3 (C-2), 171.7, 172.6 (C=O); IR (film) 1740 (C=O) cm^{-1}; MS (EI) *m/z* 187 (weak), 171 (3%), 159 (weak), 100 (2), 71 (100); Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.50; H, 8.77.

2,3-Di-(2,2-dimethylpropanoyloxy)tetrahydropyran. Tetrahydropyran-2,3-diol[26] (2.0 g, 17 mmol) was heated in dry diethyl ether with pivaloyl chloride (6.2 mL, 51 mmol), pyridine (4.2 mL, 51 mmol) and DMAP (cat.) at reflux for 3 days. The resulting mixture was allowed to cool and was then diluted with diethyl ether. It was washed with HCl (1M, 2x), saturated $NaHCO_3$ (3x) and dried ($MgSO_4$). Removal of the solvent under reduced pressure afforded a colourless oil. Flash chromatography (5% ethyl acetate / hexane) performed on this oil yielded the desired diester (0.2 g, 4%), resolved from significant amounts (≈ 0.4 g) of another product which appeared to be a monoester . The diester crystallised on standing, mp 57-60°C. ^{1}H NMR (200 MHz) δ 1.00-2.10 (m, 22H, -C(CH$_3$)$_3$, H$_2$-4, 5), 3.64-3.96 (m, 2H, H-6), 4.18-4.28 (m, 0.92H, H-3 *trans*), 4.86-4.94 (m, 0.08H, H-3 *cis*), 5.80 (d, 0.92H, J = 5 Hz, H-2 *trans*), 6.10 (d, 0.08H, J = 4 Hz, H-2 *cis*); ^{13}C NMR (75 MHz) δ 20.9 (C-5), 24.4 (C-4), 26.9 (-C(*C*H$_3$)$_3$), 38.8, 38.6 (-*C*(CH$_3$)$_3$), 62.9 (C-6), 67.3 (C-3), 91.5 (C-2), 176.9, 177.8 (C=O); MS (EI) *m/z* 271 (weak), 229 (weak), 185 (3%), 85 (23), 57 (100); (CI) *m/z* 304 (weak, (M + NH$_4$)$^+$), 287 (weak, (M + H)$^+$), 185 (100%); HRMS *m/z* 229.1076 [(M - C$_4$H$_9$)$^+$], calcd for $C_{11}H_{17}O_5$ 229.1076.

3-Butanoyloxy-2-chlorotetrahydropyran (25).[34] Tetrahydropyran-2,3-diol dibutanoate (100 mg, 0.42 mmol) was treated with $SOCl_2$ (60 mL, 0.84 mmol) and $ZnCl_2$ (≈ 20 mg) in dry benzene (2 mL) according to the procedure of Vercellotti *et al.* employed in the synthesis of glucosyl chlorides.[35] The crude product (**25**) (80 mg, 92%) was obtained as a colourless oil and used without further purification. ^{1}H NMR (200 MHz) δ 1.00 (t, 3H, J = 7Hz, -CH$_2$C*H*$_3$), 1.50-2.50 (m, 8H, -COC*H*$_2$C*H*$_2$-, H$_2$-4, 5), 3.60-4.00 (m, 2H, H$_2$-6), 4.90 (br s, 1H, H-3), 6.00 (br s, 0.6H, H-2 *trans*), 6.25 (br s, 0.4H, H-2 *cis*); ^{13}C NMR (50 MHz) δ 13.5 (-CH$_2$*C*H$_3$), 18.4 (-*C*H$_2$CH$_3$), 19.6, 21.7 (C-5), 22.6, 23.7 (C-4), 36.1 (-*C*OCH$_2$-), 61.0, 61.6 (C-6), 68.4, 69.8 (C-3), 91.4, 93.9 (C-2), 172.4, 172.7 (C=O); MS (EI) *m/z* 171 (8%), 142 (1), 1 (12), 118 (34), 100 (12), 83 (11), 71 (100).

2-Butanoyloxy-3-bromotetrahydropyran (27). Following the standard procedure,[26] 3-bromotetrahydropyran-2-ol[26] (1.0 g, 5.5 mmol) was esterified with butyryl chloride and pyridine in dry diethyl ether. The crude product (**27**) (1.2 g, 93%) was isolated as a colourless oil by means of flash chromatography (5% ethyl acetate / hexane). A sample was distilled at 60°C and 0.05 mm Hg (Kugelrohr). ^{1}H NMR (200 MHz) δ 0.98 (t, 3H, J = 7.5Hz, -CH$_2$C*H*$_3$), 1.50-2.42 (m, 8H, -COC*H*$_2$C*H*$_2$-, H$_2$-4, 5), 3.62-4.22 (m, 3H, H-3, H$_2$-6), 5.87 (d, 0.5H, J = 5.1Hz, H-2 *trans*), 6.11 (d, 0.5H, J = 2.9Hz, H-2 *cis*); ^{13}C NMR (50 MHz) δ 13.5 (-CH$_2$*C*H$_3$), 18.1, 18.2 (-*C*H$_2$CH$_3$), 23.3, 26.2 (C-5), 29.1, 30.3 (C-4), 36.0 (-CO*C*H$_2$-), 47.0, 47.2 (C-3), 60.9, 64.3 (C-6), 90.5, 94.1 (C-2), 171.5 (C=O); IR (film) 1750 (C=O), 735 (C-Br) cm^{-1}; MS (EI) *m/z* 224 (weak), 222 (weak), 206 (weak), 204 (weak), 165 (3%), 163 (3), 71 (100); (CI) *m/z* 270 (1%, (M + NH4)$^+$), 268 (1, (M + NH4)$^+$), 253 (2, (M + H)$^+$), 252 (1, M$^+$), 251 (2, (M + H)$^+$), 250 (1, M$^+$), 224 (14), 223 (16); HRMS *m/z* 164.9738 [(M - C$_3$H$_7$CO$_2$)$^+$] calcd for C$_5$H$_8$^{81}BrO.

Butanoyloxy-2-(p-tolylthio)cyclohexane (15/16). Treatment of 2-bromocyclohexanol[32] (1.0 g, 4.9 mmol) with *p*-methylthiophenol (0.6 g, 5.0 mmol) and DBU (0.9 g, 6.0 mmol) in dry benzene (130 mL), under conditions similar to those employed for the preparation of 3-(*p*-tolylthio)tetrahydropyran-2-ol,[26] yielded 2-(*p*-tolylthio)cyclohexanol as a colourless oil. The crude product was esterified with butyryl chloride and pyridine in dry diethyl ether according to the standard method.[26] Careful flash chromatography (2% ethyl acetate / hexane) performed on the product yielded the desired ester (**15/16**) (0.9 g, 63%) as a colourless oil. In total, approx. 90% of the material had *trans* geometry (**16**), however the *cis* isomer (**15**) was concentrated in the later fractions. ^{1}H NMR (200 MHz) δ 0.83-2.38 (m, 18H, -COC*H*$_2$C*H*$_2$C*H*$_3$, ArCH$_3$, H$_2$-3, 4, 5, 6), 2.96-3.12 (d of t, 0.69H, $J_{2,3}$ = 4, $J_{1,2}$ = 10Hz, H-2 *trans*), 3.22-3.36 (m, 0.31H, H-2 *cis*), 4.70-4.83 (d of t, 0.69H, $J_{1,6}$ = 5, $J_{1,2}$ = 9Hz, H-1 *trans*), 5.03-5.11 (m, 0.31H, H-1 *cis*), 7.07-7.13 (m, 2H, *o*-ArH), 7.30-7.37 (m, 2H, *m*-ArH); ^{13}C NMR (75 MHz) δ 13.4 (-CH$_2$*C*H$_3$), 18.1 (-*C*H$_2$CH$_3$), 20.8, 20.9, 23.2, 24.0, 24.6 (ArCH$_3$, C-3,4), 28.8, 29.2, 31.0, 31.3 (C-5,6), 36.1 (-CO*C*H$_2$-), 50.3, 51.1 (C-2), 71.5, 74.3 (C-1), 129.6, 129.8, 130.5, 131.6, 133.0, 133.3, 137.3, 137.4 (aromatic C), 173.2 (C=O); IR (film) 1735 (C=O) cm^{-1}; MS (EI) *m/z* 292 (1%, M$^+$), 221 (weak), 204 (20), 91 (10), 81 (64), 71 (83); HRMS *m/z* 292.1496 (M$^+$), calcd for C$_{17}$H$_{24}$O$_2$S 292.1497.

General Procedure for Bu$_3$Sn• Competition Experiments. In a typical experiment, a mixture of **11** and **12** (50 mg, 0.17 mmol), tributyltin hydride (33 mg, 85%) and AIBN (cat.) was dissolved in benzene (2 mL) containing biphenyl as an internal standard. The solution was deoxygenated with a slow stream of N$_2$ and then heated under reflux for 0.5 to 1 h. The ratio of **11** to **12** before and after the reaction was determined by capillary gas chromatography. For reactions of **13** and **14**, and **15** and **16**, ^{1}H NMR spectroscopy was used to determine the relative proportions of *cis* and *trans* isomers. This was achieved by the integration of the resonances due to H-2 at 5.77 ppm (**13**) and 6.12 ppm (**14**) [26] and the resonances between 2.9 and 3.4 ppm due to H-2 of **15** and **16**. In these later cases, the simple reduction products, 2-butanoyloxytetrahydropyran and butanoyloxycyclohexane respectively, were assumed to be the only products of the reactions.

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