Regioselectivity in the ring-opening β-scission of 2-phenyl-1,3-dioxan-2-yl radicals derived from bicyclic benzylidene acetals

Yudong Cai, Hai-Shan Dang and Brian P. Roberts*

Christopher Ingold Laboratories, Department of Chemistry, University College London, 20 Gordon Street, London, UK WC1H 0AJ

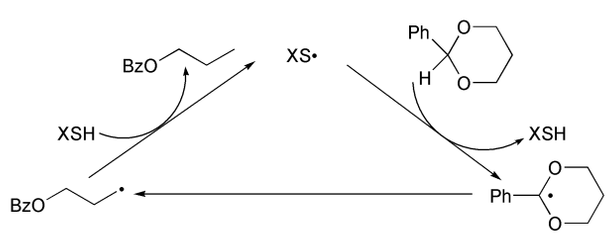
Received (in Cambridge, UK) 21st August 2002, Accepted 17th September 2002
First published as an Advance Article on the web 28th October 2002

The thiol-catalysed radical-chain redox rearrangement to benzoate esters of a number of *cis*- and *trans*-fused bicyclic benzylidene acetals derived from 1,3-diols has been investigated at *ca*. 130 °C in refluxing octane. The most generally effective and convenient combination of initiator and catalyst for this type of reaction consists of di-*tert*-butyl peroxide in conjunction with triisopropylsilanethiol. The benzoate esters are produced by β-scission of intermediate 2-phenyl-1,3-dioxan-2-yl radicals with fused cyclohexane or cyclopentane rings and there are two modes of cleavage for each radical, to give either a primary or a secondary 3-benzoyloxyalkyl radical. The regioselectivity of β-scission differs markedly depending on whether the ring junction is *cis* or *trans*, such that the *trans*-isomer gives preferentially the primary alkyl radical while the *cis*-isomer affords the secondary radical. Density functional calculations indicate that the β-scission proceeds through a product-like transition state in which the geometry at the emerging radical centre is quite close to planar. The regioselectivity observed in the β-scission of these bicyclic 1,3-dioxan-2-yl radicals can be understood in terms of the interplay between the thermodynamic driving force, charge-transfer stabilisation of the transition state and the degree of umbrella angle strain at the emerging radical centre.

We have reported recently[1,2] that cyclic benzylidene acetals derived from 1,2- and 1,3-diols undergo an efficient thiol-catalysed radical-chain redox rearrangement to give benzoate esters, as illustrated in Scheme 1 for the prototype reaction of

Scheme 1

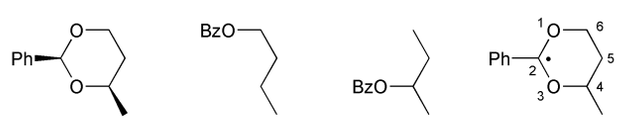
2-phenyl-1,3-dioxane **1** to give propyl benzoate. The function of the thiol is to act as a protic polarity-reversal catalyst[3,4] and thereby promote the overall transfer of a hydrogen atom between two nucleophilic carbon-centred radicals. For example, in the presence of a peroxide initiator and an alkane- or silane-thiol catalyst in refluxing octane (bp 126 °C, internal temperature *ca*. 130 °C), 2-phenyl-4-methyl-1,3-dioxane **2** was converted into a mixture of the benzoate esters **3** and **4** in the ratio 87 : 13.[1] † The propagation stage of the chain mechanism is illustrated in Scheme 2 for the unsubstituted benzylidene acetal **1**. The selective formation of the benzoate **3** from acetal **2**



Scheme 2

† Yields are sometimes improved if this type of reaction is carried out in the presence of a small amount of collidine (2,4,6-trimethylpyridine), which probably acts as a scavenger of any acid produced during the reaction (see later). Chlorobenzene can be used as solvent or co-solvent with octane if the benzylidene acetal is poorly soluble in octane alone.

results from the preference of the intermediate 2-phenyl-4-methyl-1,3-dioxan-2-yl radical **5** to undergo β-scission with cleavage of the O(3)–C(4) bond to yield a secondary alkyl radical, rather than the primary radical that results from O(1)–C(6) cleavage.

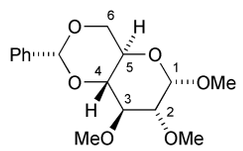


Although in this particular case it is likely that the secondary alkyl radical is thermodynamically more stable than the isomeric primary radical, as we have pointed out previously,[5] it is important not to focus exclusively on the nature of the newly formed radical centre when qualitatively judging the relative stabilities of isomeric species, such as those that arise here from the alternative modes of β-scission. Thus, it is not self-evident that the thermodynamic driving force will always favour radical-centre formation in the order tertiary > secondary > primary. It is known that, provided steric crowding is not of overriding importance, molecules that possess a branched hydrocarbon backbone are generally more stable than their straight-chain isomers,[6] particularly when electronegative atoms are attached at the site of branching,[7] and such structural features must be considered alongside the nature of the radical centre generated by bond cleavage. Thus, although the precursor of **3** is a secondary alkyl radical, it is also a *primary* alkyl benzoate and is formed by cleavage of a *polar secondary*-C–O bond. While the precursor of **4** is a primary alkyl radical, it is also a *secondary* alkyl benzoate and is formed by cleavage of a *polar primary*-C–O bond. Therefore, it is dangerous to attempt to predict which mode of β-scission will be the more favourable thermodynamically solely on the basis of the nature of the radical centre generated,[8] without considering the complex interplay between all the relevant factors.

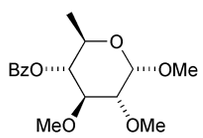
In contrast with the behaviour of **2**, redox rearrangement of

DOI: 10.1039/b208200b

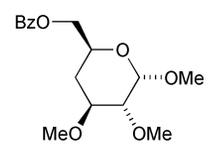
the bicyclic 4,6-*O*-benzylidene glucoside **6** yielded mainly the 6-deoxybenzoate **7**, resulting from β-scission of the intermediate dioxanyl radical to give preferentially the *primary* C(6)-centred radical, along with only a small amount of the 4-deoxybenzoate **8** (**7** : **8** = 93 : 7) that arises *via* the secondary C(4)-centred radical.[1,2] In contrast, the galactoside analogue **9** gave more **8** than **10**, indicating preferential cleavage of the intermediate dioxanyl radical to give the *secondary* C(4)-centred radical, although the selectivity (**8** : **10** = 62 : 38) was significantly less in favour of secondary-C–O cleavage than might be expected by comparison with the monocyclic dioxanyl radical **5** derived from **2**.[2]



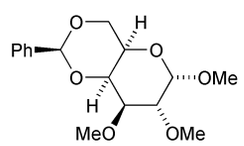
6



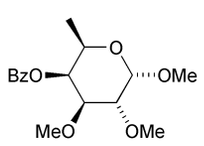
7



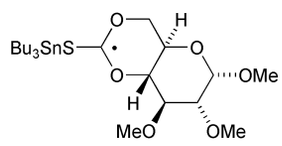
8



9

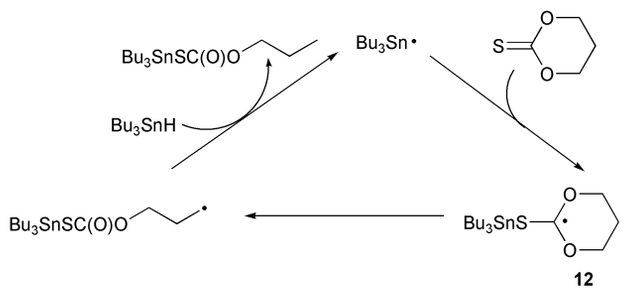


10



11

Related radical-chain reactions take place between cyclic thionocarbonates and tributyltin hydride,[8] as illustrated in Scheme 3, and here the product distribution is governed by the



12

Scheme 3

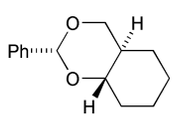
regioselectivity in the β-scission of an intermediate 2-stannyl-1,3-dioxan-2-yl radical of the type **12**. ‡ In disagreement with an earlier report,[8] we have found[2] that the intermediate radical **11** undergoes β-scission with a strong preference for formation of the primary C(6)-centred radical, rather than the secondary C(4)-centred radical, and thus the unusual regiochemistry exhibited in the redox rearrangement of the benzylidene acetal **6** is also evident in the corresponding thionocarbonate reduction. Similar counter-intuitive regioselectivity has also been reported by Ziegler and Zheng[10] for the tin hydride-mediated reductive ring opening of other bicylic thionocarbonates, as discussed later.

The aim of the present work was to investigate further the regiochemistry of the thiol-catalysed radical-chain redox rearrangement of bicyclic benzylidene acetals and to refine our preliminary ideas[2] concerning the factors that influence regioselectivity in the ring-opening β-scission of the intermediate 2-phenyl-1,3-dioxanyl radicals.

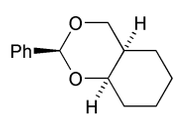
Results and discussion

Preparative studies

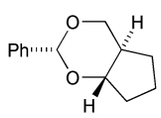
The six benzylidene acetals **13**–**18** were prepared by condensation of the appropriate racemic 1,3-diol with benzaldehyde, in the presence of pyridinium toluene-*p*-sulfonate, in refluxing benzene with azeotropic removal of the water produced. For each acetal, only one benzylidene epimer was isolated and this is assumed to be the diastereoisomer in which the phenyl group is equatorial on the 1,3-dioxane ring in the most stable conformation, although the same benzylic radical will be formed from either epimer. The acetals **13** and **14** were examined in order to probe the effects on regiochemistry of the *endo*- and *exo*-cyclic oxygen atoms associated with the pyranose rings in **6** and **9**.



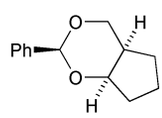
13



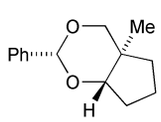
14



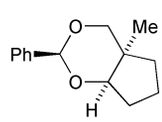
15



16



17

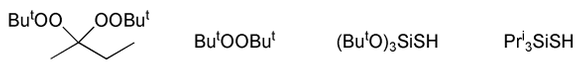


18

The general conditions we have employed previously for the redox rearrangement of benzylidene acetals involved the use of 2,2-bis(*tert*-butylperoxy)butane (BBPB) as initiator ($t_{½}$ *ca.* 1 h at 124 °C) in conjunction with tri-*tert*-butoxysilanethiol (TBST) as catalyst.[1,2] Addition of a small amount of collidine often improved yields. When the *trans*-fused [4.4.0] bicyclic acetal **13** was treated with BBPB (3 × 3 mol%) and TBST (3 × 3 mol%) in refluxing octane under argon for a total of 3 h, ^{1}H NMR spectroscopic analysis of the crude reaction product after removal of the solvent showed the presence of the benzoate esters **19** (*ca.* 60%) and **20** (*ca.* 5%), together with unchanged **13** (*ca.* 25%). However, other unidentified compounds were also present and there were NMR-spectroscopic indications that these might arise from **19** and **20** through their transesterification reactions with acidic products resulting from the decomposition of BBPB. It was found that these problems could be avoided by using di-*tert*-butyl peroxide (DTBP; $t_{½}$ *ca.* 10 h at 125 °C) as initiator. A single addition of DTBP (50 mol%) was made at the start of the reaction and the residual peroxide (bp 46–47 °C/76 mmHg) was easily removed by rotary evaporation during work up. Although TBST functioned well as the catalyst in conjunction with DTBP as initiator, triisopropylsilanethiol[11] (TIPST) proved equally effective. Both TBST and TIPST are remarkably stable to hydrolysis,[12] making them very robust silanethiol polarity-reversal catalysts but, since the latter is now available commercially, the pairing of DTBP as initiator with TIPST as catalyst is to be recommended as

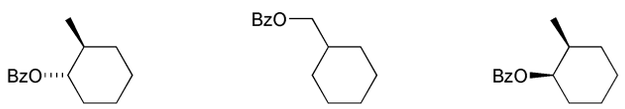
‡ We have shown[2] that triphenylsilane is a successful replacement for the tin hydride in this type of reaction and here triphenylsilanethiol, formed *in situ* as a by-product, probably serves as a polarity-reversal catalyst.[9]

the most generally effective and convenient combination for bringing about the efficient redox rearrangement of benzylidene acetals.



BBPB **DTBP** **TBST** **TIPST**

Treatment of the benzylidene acetal **13** with DTBP (50 mol%) and TIPST (5 mol%) in refluxing octane for 1.5 h brought about its clean and complete conversion to a mixture of the benzoate esters **19** and **20** (91 : 9) which could be isolated in a combined yield of 91%.§ Thus, the intermediate bicyclic 2-phenyl-1,3-dioxan-2-yl radical shows a strong preference for β-scission with cleavage of the *primary* C–O bond, in a quantitatively similar manner to the corresponding dioxanyl radical derived from the glucoside **6**, and this indicates that the oxygen atoms associated with the pyranose ring in the latter do not exert a significant influence on the regioselectivity of β-scission. In contrast, the *cis*-acetal **14** underwent clean redox rearrangement under the same conditions to afford a mixture of the benzoates **20** and **21** in the ratio 51 : 49 (combined isolated yield 92%). Thus, the 2-phenyl-1,3-dioxan-2-yl radical derived from the *cis*-acetal **14** undergoes β-scission to give both primary and secondary alkyl radicals with similar facility, paralleling the differences in regioselectivity observed for the redox rearrangements of the *trans*- and *cis*-fused carbohydrate acetals **6** and **9**. In the absence of the thiol catalyst, but under otherwise identical conditions, only 5% redox rearrangement of **14** took place.



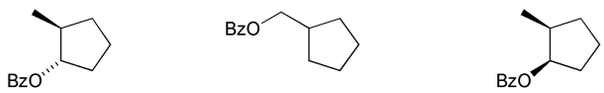
19 **20** **21**

In common with the observations for the *trans*-isomer **13**, use of BBPB as initiator (3 × 3 mol%; total reaction time 3 h) with TBST or TIPST as catalyst (3 × 3 mol%) resulted in only poor (*ca.* 45%) conversion of **14** into **20** and **21** and significant quantities of side products were also formed. Consumption of **14** increased to *ca.* 90% in the presence of collidine (10 mol%), but now the total yield of **20** and **21** was only about 70% with the remainder of the starting material accounted for as by-products.

The effect on regioselectivity of decreasing the size of the carbocyclic ring was probed through the redox rearrangement of the [4.3.0] bicyclic benzylidene acetals **15** and **16**. Rearrangement of these compounds was much faster than for the [4.4.0] analogues **13** and **14** and was complete within 30 min after only single initial additions of BBPB and TBST or TIPST (3 mol% of each); no significant amounts of by-products were detected. The reaction time could be extended to 1 h without any adverse effect on the yields of benzoates and similarly efficient rearrangement could be achieved using DTBP (50 mol%) as initiator in conjunction with TIPST (3 mol%) as catalyst. Hence, it appears that either BBPB or DTBP is a suitable initiator when the redox rearrangement is rapid, while for more sluggish rearrangements the larger amounts of BBPB and longer reaction times required lead to the production of reactive initiator-derived compounds (carboxylic acids?) that give rise to by-products, as well as sometimes resulting in inhibition of the chain-propagation cycle.

§ Increasing the thiol concentration, by adding initially 10 mol% TIPST, did not alter the ratio of **19** : **20**. This shows that interconversion of the intermediate 3-benzoyloxyalkyl radicals, by a 1,3-shift of the BzO group prior to their quenching by the thiol, is not a complicating factor.

Treatment of the *trans*-acetal **15** with BBPB and TBST in refluxing octane afforded a 98 : 2 mixture of the benzoate esters **22** and **23** in a total isolated yield of 97%. Essentially the same result was obtained using TIPST as catalyst, but in the absence of any thiol conversion was only *ca.* 5%.¶ Hence, in common with the [4.4.0] analogues, the *trans*-fused 2-phenyl-1,3-dioxanyl radical derived from **15** shows a strong preference for β-scission with cleavage of the *primary* C–O bond.



22 **23** **24**

Completely the opposite regioselectivity was found for β-scission of the dioxanyl radical derived from the *cis*-[4.3.0] acetal **16**. Thus, treatment of **16** with BBPB (3 mol%) and TBST or TIPST (3 mol%) in refluxing octane for 1 h afforded a 96 : 4 mixture of the benzoate esters **23** and **24** in a total isolated yield of 95%. Now there is a strong preference for β-scission with cleavage of the *secondary* C–O bond.

In order to compare the regiochemistry of the redox rearrangement with the regioselectivity observed by Ziegler and Zheng[10] in the reduction of a structurally similar thionocarbonate, we examined the reactions of the [4.3.0] benzylidene acetals **17** and **18** to give the benzoate esters **25** and **26**. Treatment of either acetal with BBPB and TBST (3 mol% of each) in refluxing octane for 1 h resulted in their complete conversion into the benzoate esters in total isolated yields of *ca.* 94%. NMR spectroscopic analysis of the crude reaction product showed the ratio of esters **25** : **26** to be 95 : 5 from the *trans*-acetal **17** and 3 : 97 from the *cis*-acetal **18**. Thus, the *trans*-fused [4.3.0] dioxanyl radical from **17** shows a strong preference for β-scission with cleavage of the primary C–O bond, while the *cis*-fused radical from **18** shows a similarly strong preference for cleavage of the secondary C–O bond.

25 **26**

27 **28**

29 **30**

Ziegler and Zheng have reported that the tin hydride-mediated reductive ring openings of the thionocarbonates **27** and **28** give the alcohols **29** and **30**, after hydrolysis of the first-formed *S*-stannyl thiolcarbonates (see Scheme 3).[10] These reactions, which were conducted in refluxing toluene[14] (bp 111 °C), showed regiochemistry that is remarkably similar to that found in the present work for the redox rearrangement of **17** and **18**. Thus, the ratio of alcohols **29** : **30** obtained by Ziegler and

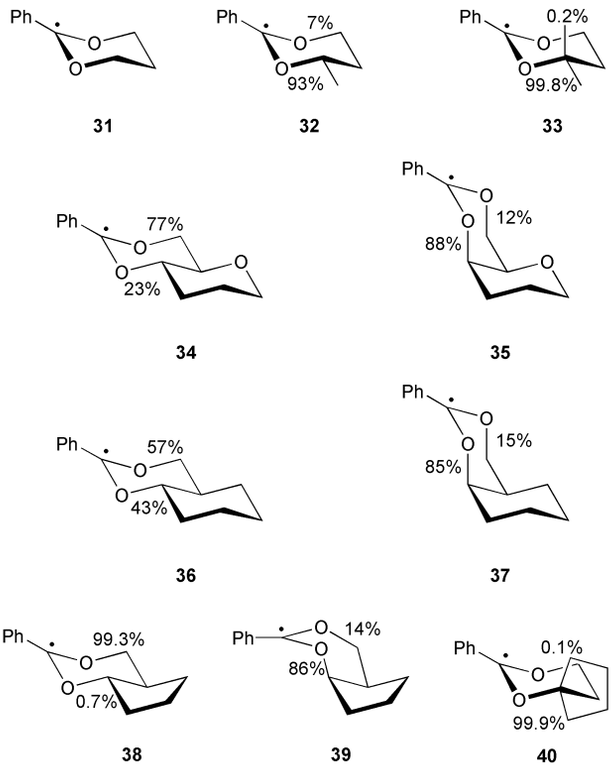
¶ No epimerisation of **15** to give **16** took place during the redox rearrangement of the former.[13] Thus, when samples were withdrawn from the reaction mixture after 10 and 15 min, the conversion of **15** to **22** and **23** was 37% and 60%, respectively, but none of the *cis*-fused isomer **16** was detectable by ^{1}H NMR spectroscopy alongside residual **15** in either case.

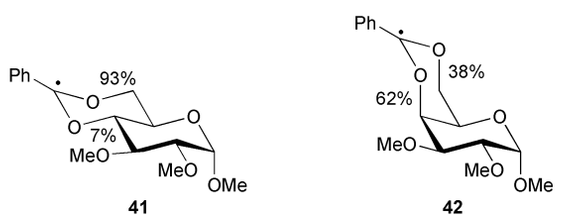
Zheng from the *trans*-fused thionocarbonate **27** was 98 : 2, while from the *cis*-fused compound **28** it was 3 : 97. The intermediate 2-stannylthiyl-1,3-dioxan-2-yl radicals (*cf.* **12** in Scheme 3) thus exhibit the same regiochemical preferences for β-scission as do the 2-phenyl analogues that are involved in the redox rearrangement of the benzylidene acetals, in accord with our previous findings for the corresponding reactions of the glucosidic acetal **6** and of the analogous thionocarbonate.[2]

Factors determining regiochemistry

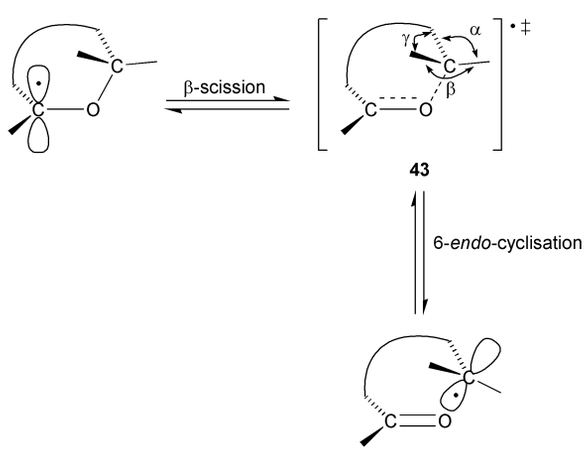
To aid interpretation of the experimental results, a series of calculations was carried out at the UB3LYP/6-31G(d,p)//UB3LYP/6-31G(d,p) level of density functional theory (DFT), using the GAUSSIAN 98 package of programs.[15] We have previously shown that DFT calculations at this level predict rates and activation energies for the β-scission of 2-phenyl-1,3-dioxanyl radicals that are in good agreement with experiment.[5] The structures of ground-state dioxanyl radicals, transition states for their β-scission and product 3-benzoyloxy radicals were fully optimised with respect to all geometrical variables without any symmetry constraints. The set of normal harmonic frequencies was computed for each structure, first in order to confirm it as a local minimum or a transition state and then to obtain the zero-point vibrational energy (ZPVE), third-law entropy and thermal contribution to the enthalpy at 298 K.[16] Preliminary molecular mechanics calculations[17] were used to determine the most stable conformation of each radical and these structures were then used as the starting points for the DFT calculations. When another conformation was predicted to be very close in energy to the ground state, this was also examined by DFT. The dioxanyl radicals **31**–**40** (most stable conformations are indicated), the transition states for their β-scission and selected product radicals were investigated; the results are summarised in Table 1. In all cases, the benzene ring lies in the OCO plane in both the ground state and the transition state. The dioxane ring is chair-like in the most stable conformations of all the dioxanyl radicals and transition structures, with the exception of the *cis*-[4.3.0] radical **39** and the associated transition states, in which it is boat-like. The alternative chair–chair conformers of the *cis*-fused [4.4.0] radicals **35** and **37**, in which the axial and equatorial substituents are interchanged, were predicted by molecular mechanics to be appreciably less stable than the conformations shown. However, the *cis*-fused structures **35** and **37** are evidently more flexible than the *trans*-fused isomers **34** and **36**, as indicated by the existence of conformations of similar energy to the ground state for the *cis*-isomers. For example, another local minimum, higher in enthalpy and free-energy than **35** by only 4.5 and 1.8 kJ mol^{-1}, respectively, was found at the DFT level. This structure differs from **35** in that the dioxanyl ring is in a twist-boat-like conformation. The computed activation parameters and rates of β-scission are collected in Table 2 and the derived regioselectivities at 130 °C are indicated alongside the relevant bonds on structures **32**–**40**.

We reported earlier[2] that, according to molecular mechanics calculations, the most stable conformation of the *trans*-fused radical **41** (derived from the glucosidic acetal **6**) is more stable than the lowest-energy conformer of the *cis*-fused analogue **42** (from the galactosidic acetal **9**) by 12.8 kJ mol^{-1} and we made use of this relative stability as part of our rationalisation for the different regiochemistry observed in the redox rearrangements of **6** and **9** (experimental regioselectivities indicated on structures **41** and **42**).[2]‖ However, a more extensive conformational search, involving exhaustive rotation of the three methoxy groups, has revealed the existence of another rotamer of **42** that is 2.6 kJ mol^{-1} *more* stable than the lowest-energy conformation of **41**. Hence, our earlier explanation must be revised and to avoid such difficulties associated with the presence of many rotatable bonds, and also make the problem more amenable to expensive high-level DFT calculations, we investigated the pair of less substituted radicals **34** and **35** as models for **41** and **42**.





The β-scission of a 2-phenyl-1,3-dioxan-2-yl radical is the reverse of 6-*endo*-cyclisation of a 3-benzoyloxyalkyl radical, as generalised in Scheme 4. We have noted previously that the transition state **43** resembles the ring-opened radical and occurs relatively 'late' along the β-scission reaction coordinate.[2,5] The C–O bond undergoing cleavage is relatively long and the



Scheme 4

‖ It should be noted that the two β-C–O bonds are aligned similarly with respect to the π SOMO in all the dioxanyl radicals considered here and thus stereoelectronic effects that depend on this alignment are unlikely to influence the regioselectivity of their β-scission, particularly in view of the 'product-like' nature of the transition states.

Table 1 Results of density functional calculations at the UB3LYP/6-31G(d,p)//UB3LYP/6-31G(d,p) level[a]

Radical[b]	Electronic energy/ hartree	Imag. freq.[c]/ cm^{-1}	r(C–O)[d]/Å	r(C=O)[e]/Å	Σ/degree	ZPVE[f,g]/ kJ mol^{-1}	$H^{g,h}$/hartree	$S^{g,h}$/ J mol^{-1} K^{-1}
31	−538.097076	None	1.437	1.365	—	498.9	−537.896215	416.0
TSP 31	−538.065238	−674.8	1.921	1.265	352.2	489.2	−537.867942	420.3
32	−577.420403	None	1.436 (p) 1.448 (s)	1.365 (p) 1.364 (s)	—	571.6	−577.190352	444.2
TSP 32	−577.387677	−669.0	1.927	1.263	352.2	561.9	−577.161230	449.1
TSS 32	−577.390800	−609.9	1.945	1.264	352.6	562.5	−577.163963	452.3
33	−616.738966	None	1.436 (p) 1.462 (t)	1.365 (p) 1.362 (t)	—	644.2	−616.479889	467.9
TSP 33	−616.705793	−681.1	1.923	1.264	352.2	634.2	−616.450379	474.9
TST 33	−616.714120	−536.7	1.953	1.264	352.4	636.1	−616.457826	477.9
34	−730.050206	None	1.438 (p) 1.438 (s)	1.367 (p) 1.368 (s)	—	681.1	−729.776846	479.7
TSP 34 (44)	−730.019719	−647.5	1.908	1.266	351.3	671.8	−729.749853	483.1
TSS 34 (45)	−730.018915	−542.3	1.927	1.267	346.6	673.5	−729.748389	482.7
35	−730.050308	None	1.432 (p) 1.442 (s)	1.362 (p) 1.365 (s)	—	681.0	−729.777062	478.6
TSP 35 (46)	−730.016767	−671.0	1.923	1.260	350.7	670.9	−729.747262	483.4
TSS 35 (47)	−730.019442	−636.3	1.934	1.263	350.6	672.0	−729.749444	485.7
36	−694.163707	None	1.439 (p) 1.442 (s)	1.365 (p) 1.365 (s)	—	744.3	−693.866006	483.7
TSP 36	−694.131468	−641.6	1.931	1.262	351.7	735.1	−693.837217	487.3
TST 36	−694.131627	−535.3	1.949	1.263	348.4	736.5	−693.836862	487.2
37	−694.163553	None	1.438 (p) 1.450 (s)	1.366 (p) 1.364 (s)	—	744.9	−693.865757	481.3
TSP 37	−694.130703	−656.5	1.939	1.263	352.2	735.1	−693.836566	485.0
TSS 37	−694.133080	−590.1	1.967	1.263	351.9	736.1	−693.838480	487.0
38	−654.832503	None	1.431 (p) 1.446 (s)	1.371 (p) 1.367 (s)	—	667.5	−654.564912	469.2
TSP 38	−654.804877	−650.5	1.916	1.267	352.4	658.6	−654.540660	472.4
TSS 38	−654.798539	−555.8	1.927	1.267	343.1	659.2	−654.534056	474.1
39	−654.838406	None	1.436 (p) 1.448 (s)	1.365 (p) 1.361 (s)	—	668.0	−654.570753	468.3
TSP 39	−654.809231	−746.2	1.886	1.270	350.2	658.7	−654.544965	476.6
TSS 39	−654.812857	−657.7	1.905	1.270	346.7	660.2	−654.548189	470.5
40	−694.156809	None	1.437 (p) 1.467 (t)	1.365 (p) 1.360 (t)	—	741.2	−693.859921	496.5
TSP 40	−694.123201	−668.2	1.932	1.263	352.3	731.0	−693.829938	505.5
TST 40	−694.134808	−549.5	1.940	1.267	352.6	734.1	−693.840648	494.5
48	−730.057469	None	—	1.216	—	669.7	−729.786815	519.5
49	−730.056903	None	—	1.216	—	672.1	−729.785475	528.3
50	−730.055861	None	—	1.217	—	669.9	−729.785256	519.0

[a] 1 Hartree = 2625.5 kJ mol^{-1}. The value of $<S^2>$ was < 0.78 for all radicals. [b] The prefixes TSP, TSS and TST denote that the structure is the transition state leading from the indicated dioxanyl radical to the primary, secondary and tertiary alkyl radical, respectively. [c] Each transition state has one imaginary vibrational mode associated with the β-scission process. [d] Length of the C–O bond that will undergo cleavage or is undergoing cleavage in the transition state. [e] Length of the C–O bond that will become a C=O double bond in the product, or the length of the developing carbonyl C=O bond in the transition state or length of the C=O bond in a product radical. [f] Negative vibrational frequencies are ignored in the calculation of ZPVE; frequencies are not scaled. [g] Low frequency normal modes are treated as vibrations, rather than rotations. Any errors caused by this approximation are expected to be small. [h] At 298.15 K.

developing C=O bond is relatively short (see Table 1 and Fig. 1). In particular, the emerging alkyl radical centre is quite close to planar in the transition structures and the degree of pyramidalisation at this centre, as measured by the sum of the bond angles Σ (= $\alpha + \beta + \gamma$), appears to be correlated with the rate of β-scission. The computed values of Σ are included in Table 1 and are remarkably constant at 352.4 ± 0.2° for the five monocyclic transition structures involved in the β-scission of **31**–**33**, even though a mix of primary, secondary and tertiary alkyl radicals is generated in these cleavage processes. We can therefore identify *umbrella angle strain* (UAS), as defined by eqn. (1), in the transition structures for β-scission of the bicyclic dioxanyl radicals.

$$\text{UAS} = 352.4° - \Sigma \qquad (1)$$

The four transition structures **44**–**47** for β-scission of **34** and **35** are displayed in Fig. 1. It is evident from the values of Σ for the two *trans*-fused transition states that the UAS is much greater in **45** that leads from **34** to the secondary alkyl radical than in **44** that leads to the primary radical. The dioxanyl

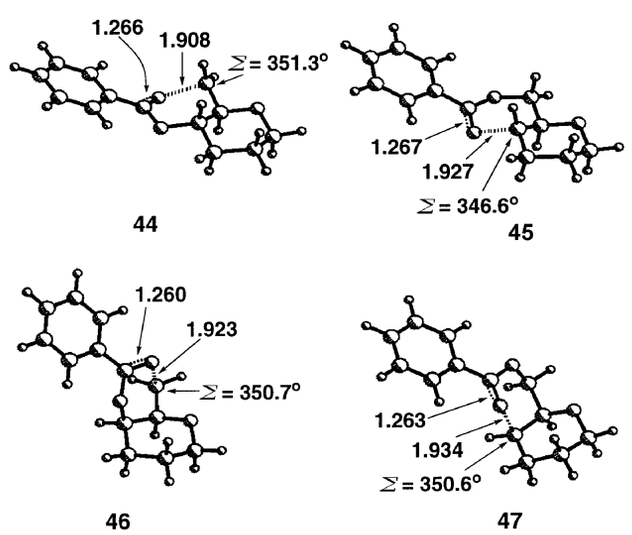


Fig. 1 DFT-computed structures of the transition states **44**–**47**. Bond lengths are given in Å.

Table 2 Computed activation parameters and rate constants for β-scission of 2-phenyl-1,3-dioxan-2-yl radicals

Reaction	$\Delta G^{\ddagger}$ [a]/kJ mol^{-1}	E_{act} [a,b]/kJ mol^{-1}	$\log_{10}(A/s^{-1})$ [c]	k_{β}/s^{-1} [d] at 130 °C	UAS/degree
31 ⟶ 1° R$^{\bullet}$	73.0	76.7	13.5	3.22×10^3	0.2
32 ⟶ 1° R$^{\bullet}$	75.0	78.9	13.5	1.78×10^3	0.2
32 ⟶ 2° R$^{\bullet}$	66.9	71.8	13.7	2.24×10^4	−0.2
32 ⟶ 2° R$^{\bullet}$ [e]	76.4	81.2	13.6	1.28×10^3	5.8
33 ⟶ 1° R$^{\bullet}$	75.4	80.0	13.6	1.69×10^3	0.2
33 ⟶ 3° R$^{\bullet}$	54.9	60.4	13.8	8.36×10^5	0.0
34 ⟶ 1° R$^{\bullet}$ (**48**)	69.9	73.3	13.4	7.84×10^3	1.1
34 ⟶ 2° R$^{\bullet}$ (**49**)	73.8	77.2	13.4	2.39×10^3	5.8
35 ⟶ 1° R$^{\bullet}$ (**50**)	76.8	80.7	13.5	1.04×10^3	1.7
35 ⟶ 2° R$^{\bullet}$ (**49**)	70.4	75.0	13.6	7.65×10^3	1.8
36 ⟶ 1° R$^{\bullet}$	74.5	78.1	13.4	1.99×10^3	0.7
36 ⟶ 2° R$^{\bullet}$	75.5	79.0	13.4	1.49×10^3	4.0
37 ⟶ 1° R$^{\bullet}$	75.6	79.1	13.4	1.46×10^3	0.2
37 ⟶ 2° R$^{\bullet}$	69.9	74.1	13.5	8.33×10^3	0.5
38 ⟶ 1° R$^{\bullet}$	62.7	66.1	13.4	6.64×10^4	0.0
38 ⟶ 2° R$^{\bullet}$	79.6	83.5	13.5	4.58×10^2	9.3
39 ⟶ 1° R$^{\bullet}$	65.2	70.2	13.7	3.69×10^4	2.2
39 ⟶ 2° R$^{\bullet}$	58.6	61.7	13.3	2.20×10^5	5.7
40 ⟶ 1° R$^{\bullet}$	76.0	81.2	13.7	1.49×10^3	0.1
40 ⟶ 3° R$^{\bullet}$	51.2	53.1	13.1	1.75×10^6	−0.2

[a] At 298.15 K. [b] Taken as equal to $\Delta H_{298}^{\ddagger} + RT$ (ref. 16). [c] Obtained from $\Delta S_{298}^{\ddagger}$ in the standard manner, as described in refs. 5 and 16. [d] Assuming E_{act} and A are independent of temperature. [e] The value of Σ in the transition state was fixed at 346.6°.

radical **32** is a monocyclic analogue of **34** and when Σ in the transition structure that leads from **32** to the secondary alkyl radical was fixed at its value in **45** (346.6°), while the remainder of the geometry was re-optimised, cleavage of the *primary* C–O bond was now predicted to occur preferentially (58 : 42%). In fact, the preference for cleavage of the primary bond shown by **34** would be expected to be greater than this, because in addition to UAS, the transition state **45** possesses strain in the tetrahydropyran ring consequent on increasing Σ to 346.6° from its value in **34** (328.7°, essentially equal to the 'tetrahedral' umbrella angle of 328.5°).

In contrast, for the *cis*-fused transition states **46** and **47** involved in the β-scission of **35**, the values of Σ are similar and correspond to relatively small amounts of UAS. We suggest that it is the increased flexibility of the *cis*-fused bicyclic framework that allows Σ to increase more easily for **35** than for the *trans*-fused **34**, removing the preference for cleavage of the primary-C–O bond shown by the latter. The predicted trends for β-scission of the model dioxanyl radicals **34** and **35** thus mirror the experimental results obtained for β-scission of the sugar-derived radicals **41** and **42**.

The computed structures of the β-scission products **48**–**50** derived from **34** and **35** are shown in Fig. 2; other conformations that differ by rotation about the BzO–C bonds are very close in energy.** Free-energy changes for the β-scission of **34** and **35** are summarised in Fig. 3, which highlights the predictions that **34** and **35** are of essentially equal stability (*cf.* the molecular mechanics results for **41** and **42**) and that the primary product radical **48** is marginally (by 0.9 kJ mol^{-1}) *more* stable than the secondary radical **49**. Entropy favours the latter and the enthalpy of **48** is actually lower than that of **49** by 3.5 kJ mol^{-1}.

Our general conclusions regarding the importance of UAS as a factor that influences the activation energies for β-scission of 1,3-dioxan-2-yl radicals are reinforced by the results obtained for the radicals **36**–**40**. While much smaller than observed experimentally (91 : 9), the preference for cleavage of the primary-C–O bond in **36** (the carbocyclic analogue of **34**) is also predicted by the DFT calculations, in accord with the relatively large UAS of 4.0° present in the transition state for secondary-C–O cleavage of **36**. For the corresponding *cis*-fused radical **37**, a much greater proportion of secondary-C–O cleavage is predicted (85%) and found by experiment (51%), consistent with the small and very similar values of the UAS in both transition states for β-scission of this more flexible *cis*-fused dioxanyl radical.

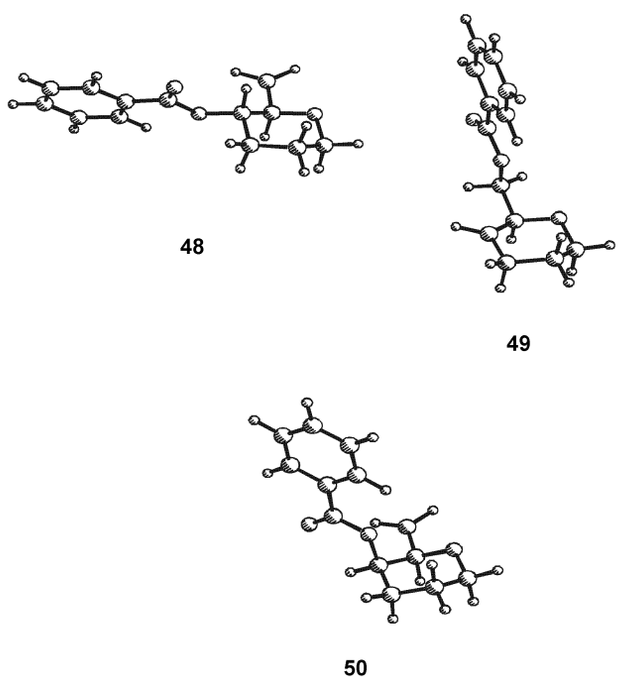


Fig. 2 DFT-computed structures of the 3-benzoyloxyalkyl radicals formed by β-scission of the 1,3-dioxanyl radicals **34** and **35**.

When the size of the attached fused carbocyclic ring is decreased from 6 to 5 atoms in the dioxanyl radicals **38** and **39**, the preference of the *trans*-fused isomer to give the primary alkyl radical, while the *cis*-isomer favours the secondary radical, is increased. For β-scission of the *trans*-dioxanyl radical **38**, the UAS values for cleavage of the primary- and secondary-C–O bonds are 0.0 and 9.3°, respectively, and the large UAS associated with production of the secondary alkyl radical is reflected in the strong preference for primary-C–O cleavage. However, the corresponding UAS value for secondary-C–O cleavage of the more flexible *cis*-fused isomer is only 3.5° larger than for cleavage of the primary-C–O bond and the primary : secondary cleavage ratio is now in favour of the secondary radical (4 : 96 by experiment, 14 : 86 calculated).

** Note that, because the R–OBz and PhC=O bonds are not in a *cis*-coplanar arrangement, stabilising 'ester resonance' will not be as fully developed in the transition states for β-scission as the product-like nature of the latter might imply.

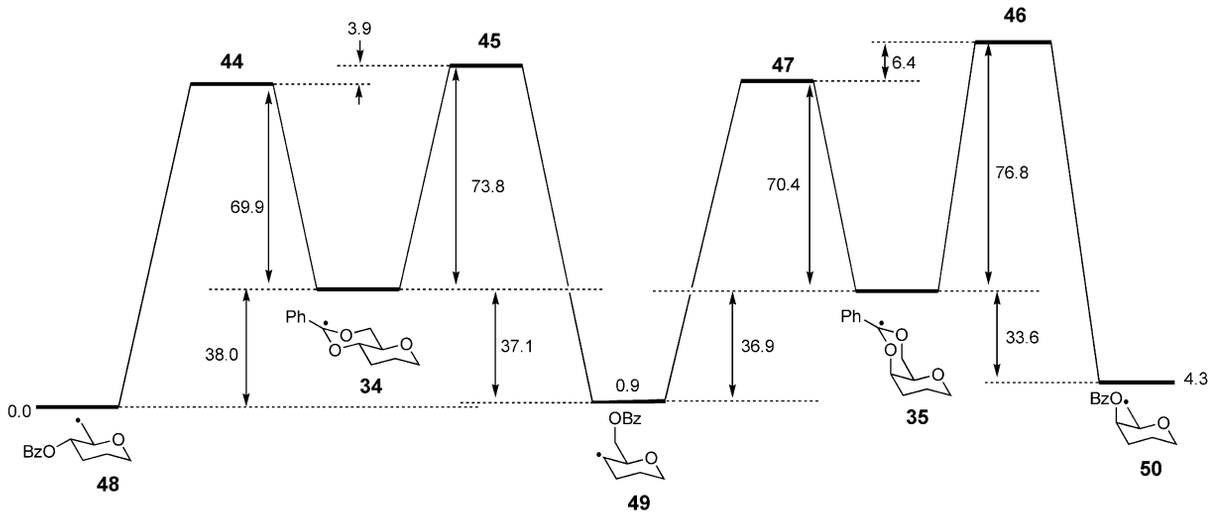
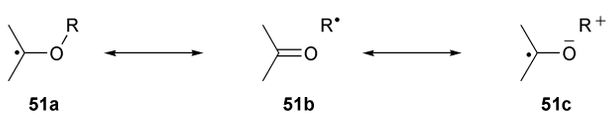


Fig. 3 DFT-computed free-energy changes (kJ mol^{-1} at 298.15 K) associated with the β-scission of the 1,3-dioxanyl radicals **34** and **35**.

The case of the spirocyclic radical **40** is interesting because, unlike the edge-fused bicyclic structural isomers **38** and **39**, experiments show[5] that the corner-fusion of the 5-membered ring at the emerging radical centre does not reduce the relative rate of cleavage of the tertiary-C–O bond as compared with the primary-C–O bond. Indeed, cleavage to form the tertiary alkyl radical takes place somewhat *more* rapidly for **40** than for the non-spirocyclic analogue **33**[5] and these relative rates of β-scission are reproduced by the DFT calculations (see Table 2). The values of Σ in the transition states for cleavage of either primary- or tertiary-C–O bonds in **40** are virtually identical and correspond to effectively zero UAS.

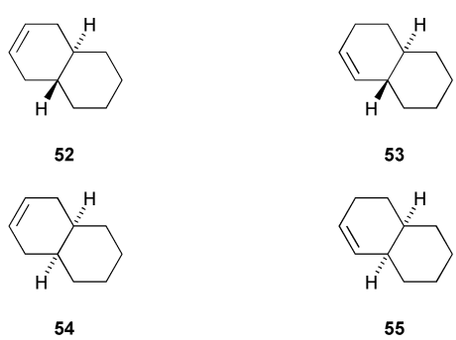
Conclusion

The β-scission of cyclic 2-phenyl-1,3-dioxan-2-yl radicals proceeds *via* a product-like transition state and there is a basic tendency for the rate of bond cleavage to follow the order 1° C–O < 2° C–O < 3° C–O. This trend probably arises from a combination of differences in thermodynamic driving force and charge-transfer stabilisation of the transition state, as represented by inclusion of structure **51c** in a valence-bond description of the latter. However, in fused bicyclic systems, where the shape of the emerging bridgehead carbon-radical centre in the transition state is constrained, umbrella angle strain at this centre appears to become of critical importance and may often be the dominant factor governing regioselectivity.



The *cis*-fused [4.4.0] and [4.3.0] bicyclic frameworks are more flexible than their *trans*-fused counterparts and thus the preferred umbrella angle Σ is more easily accommodated in the transition states for β-scission of the *cis*-fused dioxanyl radicals. Consequently, while the *trans*-fused bicyclic radicals show a preference for β-scission with cleavage of 1° C–O bonds, the 'usual' 2° C–O > 1° C–O order is shown by the *cis*-analogues although, for the [4.4.0] radicals, the preference for secondary-C–O cleavage is still less marked than for the comparable unconstrained monocyclic radical **5**.

Because of the complex interplay between all the various interactions involved, it is notoriously difficult to apportion the total strain energy of a molecule *quantitatively* between its various components and it can be hazardous to suggest that strain is localised in a particular part of a molecule. Although we believe that the evidence supports the importance of umbrella angle strain, it is of interest to note that the relative stabilities of the bicyclic [4.4.0] transition states **44**–**47** show a general parallel with those of the octalins **52**–**55**.[18] †† Thus, in agreement with approximate estimates based on experimental data,[18] molecular mechanics calculations[17,18c] predict that the enthalpy of formation of the *trans*-fused Δ^2-isomer **52** is *lower* by 2.9 kJ mol^{-1} than that of the Δ^1-isomer **53**. However, for the *cis*-fused octalins, the enthalpy of formation of the Δ^2-isomer **54** is *higher* than that of the Δ^1-isomer **55** (vinyl group axial ‡‡) by 0.4 kJ mol^{-1} and the relative stabilities of the pairs of *cis*- and *trans*-octalins have been interpreted in terms of differences in torsional/van der Waals interactions.[18a,b] To the extent that these bicyclic alkenes may be considered as models for the late transition states **44**–**47**, this could be taken to suggest that more emphasis should be to given to torsional and van der Waals strain as factors determining the relative stabilities of **44**–**47** (and thus the rates of the competing modes of β-scission).



With regard to the reductive ring opening of cyclic thionocarbonates mediated by tin hydrides,[2,8] it seems likely that the same factors will control regioselectivity in the β-scission of the intermediate 2-stannylthio-1,3-dioxan-2-yl radicals (*e.g.* **11** and **12**) and that cleavage also proceeds *via* a product-like transition state.

Experimental

NMR spectra were recorded using a Bruker AVANCE 500 instrument (500 MHz for ^{1}H, 125.7 MHz for ^{13}C). The solvent was $CDCl_3$ and chemical shifts are reported relative to residual

†† We are grateful to Professor W. B. Motherwell for drawing our attention to this analogy.

‡‡ The isomer with the vinyl group equatorial is more stable by 2.7 kJ mol^{-1}.

$CHCl_3$ (δ_H = 7.26) or to $CDCl_3$ (δ_C = 77.0 ppm); *J* values are quoted in Hz and the use of [multiplet] indicates an apparent multiplet associated with an observed line spacing. Column chromatography and TLC were carried out using Merck Kieselgel 60 (230–400 mesh) and Kieselgel 60 F_{254} aluminium-backed pre-coated plates, respectively.

All manipulations and reactions of air-sensitive compounds were carried out under an atmosphere of dry argon or nitrogen and all extracts were dried over anhydrous $MgSO_4$. Light petroleum refers to the fraction of bp 40–60 °C.

Materials

Anhydrous octane, 2,2-bis(*tert*-butylperoxy)butane (50% w/w in mineral oil) and di-*tert*-butyl peroxide (98%) were obtained commercially (Aldrich) and were used as received. Tri-*tert*-butoxysilanethiol was prepared according to a modification of the literature method,[19] as described previously,[13] and tri-isopropylsilanethiol was prepared according to the method of Soderquist and co-workers.[11]

The *cis*- and *trans*-isomers of 2-hydroxymethylcyclohexanol were prepared separately by $LiAlH_4$-reduction of ethyl *cis*- or *trans*-2-hydroxycyclohexanecarboxylate, respectively, themselves prepared as a mixture by the $NaBH_4$-reduction of ethyl 2-oxocyclohexanecarboxylate (Fluka) and separated by column chromatography.[20] The ^1H NMR spectra agreed with the reported data;[20] δ_C (*cis*) 20.5, 23.5, 24.9, 32.7, 42.4, 65.7, 69.3; δ_C (*trans*) 24.4, 25.0, 27.2, 35.4, 46.1, 68.9, 76.6.

The *cis*- and *trans*-isomers of 2-hydroxymethylcyclopentanol[21] were prepared as a 42 : 58 mixture by $LiAlH_4$-reduction of ethyl 2-oxocyclopentanecarboxylate (Aldrich), as described in the literature.[22] The isomeric mixture was separated by column chromatography, eluting first with CH_2Cl_2–diethyl ether (5 : 1), followed by chloroform and finally chloroform–methanol (10 : 1). The *cis*-isomer showed δ_H 1.50–2.20 (7 H, complex, ring H), 2.50 (2 H, br s, OH), 3.81 (2 H, m, CH_2O), 4.41 (1 H, m, H-1); δ_C 22.4, 25.6, 35.6, 45.8, 63.1, 75.4. The *trans*-isomer showed δ_H 1.18–2.09 (7 H, complex, ring H), 2.20 (2 H, br s, OH), 3.56 (1 H, dd, *J* 10.3 and 8.9, CH^AH^BO), 3.78 (1 H, dd, *J* 10.3 and 5.3, CH^AH^BO), 4.03 (1 H, [q], *J* 6.7, H-1); δ_C 21.6, 26.1, 34.4, 49.5, 66.3, 78.0.

A mixture of the *cis*- and *trans*-isomers of 2-hydroxymethyl-2-methylcyclopentanol[23] was prepared by $LiAlH_4$-reduction of ethyl 2-methyl-2-oxocyclopentanecarboxylate,[24] using a modification of the literature procedure,[23a] as follows. Ethyl 2-methyl-2-oxocyclopentanecarboxylate (20.5 g, 0.12 mol) was added cautiously dropwise over 30 min to a stirred suspension of $LiAlH_4$ (6.50 g, 0.17 mol) in refluxing tetrahydrofuran (250 mL). The reaction mixture was heated under reflux for a further 1 h, allowed to cool and treated successively with water (6.5 mL), aqueous sodium hydroxide (15% w/v, 6.5 mL) and water (6.5 mL). After removal of the precipitate by filtration through Celite, concentration of the filtrate afforded a mixture of the *cis*- and *trans*-diols in the ratio 30 : 70. If the reduction was carried out at ice-bath temperature,[22a] this ratio was only 10 : 90. The mixture of diols was separated by column chromatography, eluting first with CH_2Cl_2–diethyl ether (5 : 1), followed by chloroform and finally chloroform–methanol (10 : 1) to give the *cis*-isomer (3.20 g, 21%) as an oil from the earlier fractions; δ_H 0.96 (3 H, s, Me), 1.28 (1 H, m, ring-H), 1.61 (2 H, m, CH_2), 1.76 (2 H, m, CH_2), 2.01 (1 H, m, ring-H), 2.60 (2 H, br s, OH), 3.56 (1 H, d, *J* 11.1, CH^AH^BOH), 3.70 (1 H, d, *J* 11.1, CH^AH^BOH), 3.91 (1 H, m, H-1); δ_C 21.2, 23.2, 33.4, 34.6, 46.3, 68.6, 82.1.

The *trans*-isomer was obtained as an oil (8.20 g, 53%) from the later fractions; δ_H 0.97 (3 H, s, Me), 1.40 (2 H, m, CH_2), 1.55 (2 H, m, CH_2), 1.57 (1 H, m, ring-H), 2.00 (1 H, m, ring-H), 2.50 (2 H, br s, OH), 3.42 (1 H, d, *J* 10.4, CH^AH^BOH), 3.51 (1 H, d, *J* 10.4, CH^AH^BOH), 3.96 (1 H, m, H-1); δ_C 16.4, 19.0, 31.9, 33.3, 45.4, 71.5, 78.5.

Preparation of the benzylidene acetals 13–18

A mixture of the diol (typically *ca.* 17 mmol), benzaldehyde (2.0 g, 19 mmol) and pyridinium toluene-*p*-sulfonate (50 mg) in benzene (40 mL) was stirred and heated under reflux for *ca.* 1 h, while water was separated using a Dean–Stark trap. The solution was allowed to cool, shaken with calcium carbonate (200 mg) to neutralise the acid and the suspension was filtered through Celite. The filter cake was washed with diethyl ether, the solvent was removed from the filtrate by evaporation and the acetals were isolated, as oils unless stated otherwise, by flash chromatography (light petroleum–diethyl ether eluent 10 : 1) usually followed by distillation under reduced pressure. The characteristic properties are given below.

Acetal 13 from *trans*-2-hydroxymethylcyclohexanol[25]

White crystals from hexane–methanol (yield 89%), mp 63–64 °C; δ_H 0.96 (1 H, [q], *J* 12.6 and 3.8, ring-H), 1.25–1.43 (2 H, m, ring-H), 1.45–1.60 (2 H, m, ring-H), 1.75 (2 H, m, ring-H), 1,87 (1 H, m, ring-H), 2.00 (1 H, m, ring-H), 3.47 (1 H, ddd, *J* 11.0, 9.9 and 4.3, bridgehead-CHO), 3.58 (1 H, [t], *J* 11.0, CH^AH^BO), 4.10 (1 H, dd, *J* 11.0 and 4.3, CH^AH^BO), 5.58 (1 H, s, PhCH), 7.35 (3 H, m, Ph), 7.51 (2 H, m, Ph); δ_C 24.7, 25.1, 26.1, 31.6, 41.0, 72.1, 82.0, 101.8, 126.2, 128.3, 128.7, 138.7. (Found: C, 76.9; H, 8.2. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%).

Acetal 14 from *cis*-2-hydroxymethylcyclohexanol

Yield 90%, bp 106–108 °C/0.05 mmHg (solidified during storage in a refrigerator, mp 35 °C); δ_H 1.31 (1 H, [qt], *J* 13.2 and 3.6, ring-H), 1.43 (1 H, m, ring-H), 1.52 (3 H, m, ring-H), 1.64 (1 H, m, ring-H), 1.83 (1 H, m, ring-H), 2.00 (1 H, m, ring-H), 2.16 (1 H, [q]d, *J* 13.2 and 3.6, ring-H), 3.93 (1 H, br d, *J* 11.2, CH^AH^BO), 4.06 (1 H, dd, *J* 11.2 and 2.8, CH^AH^BO), 4.10 (1 H, br m, bridgehead-CHO), 5.52 (1 H, s, PhCH), 7.34 (3 H, m, Ph), 7.53 (2 H, m, Ph); δ_C 20.2, 24.7, 25.5, 31.7, 35.4, 72.4, 74.9, 101.9, 126.3, 128.3, 128.8, 139.1. (Found: C, 76.9; H, 8.2. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%).

Acetal 15 from *trans*-2-hydroxymethylcyclopentanol

Yield 94%, bp 93–95 °C/0.07 mmHg (solidified during storage in a refrigerator, mp 39–40 °C); δ_H 1.15 (1 H, m, ring-H), 1.60–1.90 (5 H, complex, ring-H), 2.05 (1 H, m, ring-H), 3.52 (1 H, td, *J* 10.5 and 7.1, bridgehead-CHO), 3.74 (1 H, t, *J* 10.5, CH^AH^BO), 4.43 (1 H, dd, *J* 10.5 and 4.2, CH^AH^BO), 5.52 (1 H, s, PhCH), 7.36 (3 H, m, Ph), 7.54 (2 H, m, Ph); δ_C 18.6, 22.4, 28.3, 41.7, 73.1, 83.8, 101.7, 126.2, 128.2, 128.8, 138.3. (Found: C, 76.2; H, 7.8. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.9%).

Acetal 16 from *cis*-2-hydroxymethylcyclopentanol

Yield 92%, bp 95–98 °C/0.05 mmHg; δ_H 1.50–2.40 (7 H, complex, ring-H), 4.14 (1 H, br d, *J* 11.6, CH^AH^BO), 4.21 (1 H, dd, *J* 11.6 and 2.8, CH^AH^BO), 4.32 (1 H, [t], *J* 3.5, bridgehead-CHO), 5.45 (1 H, s, PhCH), 7.36 (3 H, m, Ph), 7.48 (2 H, m, Ph); δ_C 22.7, 25.6, 33.1, 39.4, 67.6, 80.1, 100.4, 126.1, 128.2, 128.7, 138.9. (Found: C, 76.2; H, 7.8. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.9%).

Acetal 17 from *trans*-2-hydroxymethyl-2-methylcyclopentanol

Yield 87%, bp 90–92 °C/0.07 mmHg; δ_H 1.14 (3 H, s, Me), 1.23 (1 H, m, ring-H), 1.45 (1 H, m, ring-H), 1.68 (2 H, m, ring-H), 1.79 (1H, m, ring-H), 1.93 (1 H, m, ring-H), 3.55 (1 H, dd, *J* 11.2 and 7.6, bridgehead-CHO), 3.72 (1 H, d, *J* 10.2, CH^AH^BO), 4.15 (1 H, d, *J* 10.2, CH^AH^BO), 5.51 (1 H, s, PhCH), 7.36 (3 H, m, Ph), 7.53 (2 H, m, Ph); δ_C 16.5, 17.0, 25.2, 30.0, 38.2, 79.8, 84.8, 102.6, 126.3, 128.3, 128.7, 138.3. (Found: C, 76.8; H, 8.4. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%).

Acetal 18 from *cis*-2-hydroxymethyl-2-methylcyclopentanol

Yield 88%, bp 90–92 °C/0.06 mmHg; δ_H 0.84 (3 H, s, Me,), 1.35 (1 H, m, ring-H), 1.81 (2 H, m, ring-H), 2.00 (2 H, m, ring-H), 2.37 (1 H, m, ring-H), 3.78 (1 H, d, *J* 11.6, C*H*^{A}H^{B}O), 3.88 (1 H, br d, *J* 3.9, bridgehead-CHO), 3.95 (1 H, d, *J* 11.6, CH^A*H*^{B}O), 5.43 (1 H, s, PhCH), 7.37 (3 H, m, Ph), 7.51 (2 H, m, Ph); δ_C 20.9, 21.2, 30.9, 31.5, 41.1, 72.9, 85.9, 100.6, 126.2, 128.3, 128.8, 138.9. (Found: C, 76.8; H, 8.4. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%).

General procedure for redox rearrangement of benzylidene acetals

The acetal (2.0 mmol), dry octane (2.5 mL), initiator (0.06 mmol if BBPB, 1.0 mmol if DTBP) and thiol catalyst (0.06–0.10 mmol) were successively introduced into an argon-filled 10 cm^3 two-necked round-bottomed flask, containing a dry magnetic stirrer bar and fitted with a condenser through which a slow downward flow of argon was maintained. The side neck was closed with a stopper and the flask was immersed in an oil bath that had been pre-heated to 140–145 °C. The mixture was stirred under reflux for 1–3 h, allowed to cool and the octane was removed by evaporation under reduced pressure. The crude product was examined by ^{1}H NMR spectroscopy to determine its composition and estimate the extent of conversion to benzoate esters, before the latter were isolated by flash chromatography (light petroleum–diethyl ether eluent 10 : 1). When further additions of initiator and/or thiol were made to the reaction mixture, the flask was raised from the oil bath and allowed to cool briefly before the reagents were added quickly through the side neck. Further additions were made at *ca.* 20–30 min intervals and reflux was continued for 1–2 h after the last addition. The NMR spectroscopic data for the benzoate esters are given below and were in accord with data in the literature (where available), although the isomeric mixtures obtained (all oils) from each benzylidene acetal were not separated.

***trans*-2-Methylcyclohexyl benzoate 19**[26]

δ_H 0.96 (3 H, d, *J* 6.5, Me,), 1.15 (1 H, m, ring-H), 1.28 (1 H, m, ring-H), 1.40 (2 H, m, ring-H), 1.69 (2 H, m, ring-H), 1.81 (2 H, m, ring-H), 2.10 (1 H, m, ring-H), 4.66 (1 H, [t]d, *J* 10.0 and 4.4, H-1), 7.43 (2 H, m, Ph), 7.54 (1 H, m, Ph), 8.06 (2 H, m, Ph); δ_C 18.5, 24.7, 25.3, 31.7, 33.5, 37.4, 79.0, 128.3, 129.5, 130.9, 132.7, 166.3.

Cyclohexylmethyl benzoate 20[27]

δ_H 1.00–1.90 (11 H, complex, ring-H), 4.13 (2 H, d, *J* 6.4, CH_2O), 7.44 (2 H, m, Ph), 7.55 (1 H, m, Ph), 8.06 (2 H, m, Ph); δ_C 21.1, 25.7 (2 C), 26.4, 29.8 (2 C), 70.1, 128.3, 129.5, 130.6, 132.7, 166.1.

***cis*-2-Methylcyclohexyl benzoate 21**[28]

δ_H 0.95 (3 H, d, *J* 6.9, Me,), 1.01–1.90 (9 H, complex, ring-H), 5.20 (1 H, m, H-1), 7.44 (2 H, m, Ph), 7.55 (1 H, m, Ph), 8.08 (2 H, m, Ph); δ_C 17.6, 24.8, 29.6, 29.9, 35.0, 37.3, 74.4, 128.3, 129.6, 131.0, 132.8, 166.7.

***trans*-2-Methylcyclopentyl benzoate 22**[29]

δ_H 1.06 (3 H, d, *J* 6.9, Me), 1.27 (1 H, m, ring-H), 1.75 (3 H, m, ring-H), 1.98 (1 H, m, ring-H), 2.11 (1 H, m, ring-H), 2.22 (1 H, m, ring-H), 4.95 (1 H, m, H-1), 7.43 (2 H, m, Ph), 7.54 (1 H, m, Ph), 8.03 (2 H, m, Ph); δ_C 18.3, 22.5, 31.4, 31.9, 40.1, 83.2, 128.2, 129.5, 130.8, 132.7, 166.5.

Cyclopentylmethyl benzoate 23[30]

δ_H 1.35 (2 H, m, ring-H), 1.61 (4 H, m, ring-H), 1.82 (2 H, m, ring-H), 2.35 (1 H, [septet], *J* 7.1, quaternary-CH), 4.21 (2 H, d, *J* 7.1, CH_2O), 7.44 (2 H, m, Ph), 7.55 (1 H, m, Ph), 8.04 (2 H, m, Ph); δ_C 25.4 (2 C), 29.4 (2 C), 38.6, 68.9, 128.3, 129.5, 130.5, 132.8, 166.7.

***cis*-2-Methylcyclopentyl benzoate 24**[29]

Present only in small amounts in admixture with **22**: δ_H 1.05 (3 H, d, *J* 6.9, Me), 1.40–2.25 (7 H, m, ring-H), 5.27 (1 H, m, H-1), 7.44 (2 H, m, Ph), 7.55 (1 H, m, Ph), 8.04 (2 H, m, Ph).

The benzoate esters **25** and **26** appear not to have been reported previously.

2,2-Dimethylcyclopentyl benzoate 25

Contains *ca.* 4% of the isomer **26**; δ_H 1.04 (3 H, s, Me), 1.09 (3 H, s, Me), 1.52 (1 H, m, ring-H), 1.65–1.90 (4 H, m, ring-H), 2.23 (1 H, m, ring-H), 4.98 (1 H, dd, *J* 6.4 and 4.1, H-1), 7.44 (2 H, m, Ph), 7.55 (1 H, m, Ph), 8.04 (2 H, m, Ph); δ_C 20.1, 22.5, 26.7, 30.7, 38.2, 42.3, 83.5, 128.3, 129.5, 130.9, 132.7, 166.3. (Found: C, 77.1; H, 8.4. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%).

1-Methylcyclopentylmethyl benzoate 26

Contains *ca.* 3% of the isomer **25**; δ_H 1.13 (3 H, s, Me), 1.43 (2 H, m, ring-H), 1.60–1.75 (6 H, m, ring-H), 4.11 (2 H, s, CH_2O), 7.45 (2 H, m, Ph), 7.56 (1 H, m, Ph), 8.05 (2 H, m, Ph); δ_C 25.3(6), 25.4(0) (2 C), 37.1 (2 C), 43.0, 73.0, 128.6, 129.9, 131.0, 133.2, 167.2. (Found: C, 77.2; H, 8.4. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%).

Acknowledgements

We acknowledge support from the EPSRC for this work.

References

1 B. P. Roberts and T. M. Smits, *Tetrahedron Lett.*, 2001, **42**, 137.
2 B. P. Roberts and T. M. Smits, *Tetrahedron Lett.*, 2001, **42**, 3663.
3 B. P. Roberts, *Chem. Soc. Rev.*, 1999, **28**, 25.
4 H.-S. Dang and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1161 and references cited therein.
5 A. J. Fielding, P. Franchi, B. P. Roberts and T. M. Smits, *J. Chem. Soc., Perkin Trans. 2*, 2002, 155.
6 S. W. Benson and M. Luria, *J. Am. Chem. Soc.*, 1975, **97**, 704.
7 (*a*) N. Laurencelle and P. D. Pacey, *J. Am. Chem. Soc.*, 1993, **115**, 625; (*b*) B. P. Roberts and A. J. Steel, *J. Chem. Soc., Perkin Trans. 2*, 1994, 2155; (*c*) J. N. Harvey and H. G. Viehe, *J. Prakt. Chem.*, 1995, **337**, 253; (*d*) B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 1996, 2719; (*e*) Y.-R. Luo and S. W. Benson, *J. Phys. Chem. A*, 1997, **101**, 3042; (*f*) A. A. Zavitsas, *J. Chem. Educ.*, 2001, **78**, 417.
8 D. H. R. Barton and R. Subramanian, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1718.
9 Y. Cai and B. P. Roberts, *Tetrahedron Lett.*, 2001, **42**, 763.
10 F. E. Ziegler and Z. Zheng, *J. Org. Chem.*, 1990, **55**, 1416.
11 E. I. Miranda, M. J. Diaz, I. Rosado and J. A. Soderquist, *Tetrahedron Lett.*, 1994, **35**, 3221.
12 Y. Cai and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 2002, 1858.
13 H.-S. Dang, B. P. Roberts and D. A. Tocher, *J. Chem. Soc., Perkin Trans. 1*, 2001, 2452.
14 F. E. Ziegler, personal communication.
15 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, N. Rega, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle and J. A. Pople, GAUSSIAN 98, revision A.11.3, Gaussian, Inc., Pittsburgh PA, 2002.
16 H. Maskill, *The Physical Basis of Organic Chemistry*, Oxford University Press, Oxford, 1990.

17 Using the MMX force-field incorporated in PCMODEL version 7.5, Serena Software, Bloomington, IN 47402-3076, USA.
18 (*a*) N. L. Allinger, J. A. Hirsch, M. A. Miller and I. J. Tyminski, *J. Am. Chem. Soc.*, 1968, **90**, 5773; (*b*) F. Johnson, *Chem. Rev.*, 1968, **68**, 375; (*c*) J. W. Huffman and W. H. Blake, *J. Org. Chem.*, 1988, **53**, 3828; (*d*) H. W. Thompson and K. D. Gaglani, *J. Chem. Soc., Perkin Trans. 2*, 1993, 967.
19 V. R. Piekos and W. Wojnowski, *Z. Anorg. Allg. Chem.*, 1969, **318**, 212.
20 O. Kanno and I. Kawamoto, *Tetrahedron*, 2000, **56**, 5639.
21 H. Favre and J. P. Lapointe, *Can. J. Chem.*, 1971, **49**, 3851.
22 Y. Huang, A. E. Sopchik, A. M. Arif and W. G. Bentrude, *J. Am. Chem. Soc.*, 1993, **115**, 4031.
23 (*a*) M. Matsumoto, H. Shirahama, A. Ichihara, H. Shin, S. Kagawa, F. Sakan, S. Noshida, S. Matsumoto, K. Saito and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 1140; (*b*) C. L. Penney and B. Belleau, *Can. J. Chem.*, 1978, **56**, 2396.
24 K. Sato, S. Susuki and Y. Kojima, *J. Org. Chem.*, 1967, **32**, 339.
25 F. A. Luzzio and R. A. Bobb, *Tetrahedron Lett.*, 1997, **38**, 1733.
26 (*a*) T. Oriyama, Y. Hori, K. Imai and R. Sasaki, *Tetrahedron Lett.*, 1996, **37**, 8543; (*b*) K. S. Ng, J. L. Roberts, P. S. Rutledge, M. A. Wilson and P. D. Woodgate, *Aust. J. Chem.*, 1976, **29**, 2683.
27 M. Nishiki, H. Miyataka, Y. Niino, N. Mitsuo and T. Satoh, *Tetrahedron Lett.*, 1982, **23**, 193.
28 M. Julia, F. L. Goffic and L. Katz, *Bull. Soc. Chim. Fr.*, 1964, 1122.
29 A. G. M. Barrett, D. C. Braddock, R. A. James, N. Koike and P. A. Procopiou, *J. Org. Chem.*, 1998, **63**, 6273.
30 R. D. Rieke, W. R. Klein and T.-C. Wu, *J. Org. Chem.*, 1993, **58**, 2492.