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Radical Reactions of Bicyclo[2.2.1]heptan-3-spiro-2'-oxiranes

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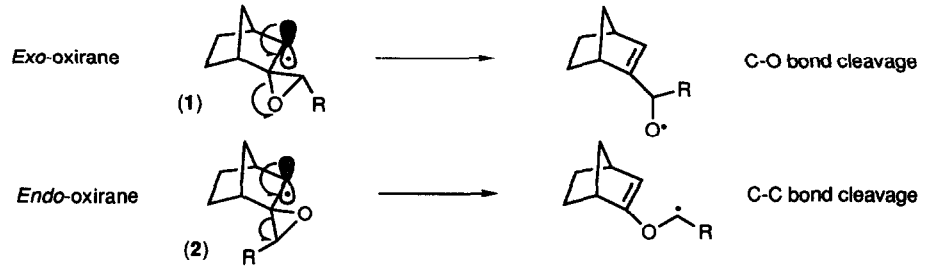
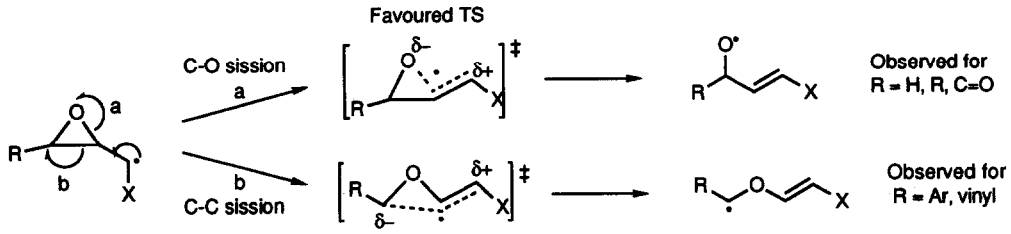
Abstract: *Tributyltin hydride reduction of 2-bromo- and 2-keto-bicyclo[2.2.1]heptan-3-spiro-2'-oxiranes gives ring opening of the oxirane-rings via intermediate 3-(spiro-2'-oxiranyl)bicyclo[2.2.1]heptan-2-yl radicals, whereas reduction of the analogous 2-(thiocarbonyl)imidazolides) [2-(O-CS-Im)] unusually yields the 2-methoxy derivatives and does not proceed by the expected normal fragmentation to yield 3-(spiro-2'-oxiranyl)bicyclo[2.2.1]heptan-2-yl radicals and subsequent ring-opening of the oxirane rings.*

As part of our ongoing studies[1] on the stereoselectivity of the ring-opening of α-oxiranylcarbinyl radicals, we have investigated the reactions of 3-(spiro-2'-oxiranyl)bicyclo[2.2.1]heptan-2-yl radicals. The expectation was that the ring-opening of the oxirane would favour C-O bond cleavage for the *endo*-oxiranes (**1**) and C-C bond cleavage for the *exo*-oxiranes (**2**) as shown in Scheme 1. The prediction was based on the stereoelectronic control observed[2,3] for α-cyclopropyl- and α-cyclobutyl-carbinyl radicals. The observed stereoelectronic control the ring-opening of these radicals is explained by the requirement in the transition state (TS) (see Scheme 2) for the semi-occupied *p*-molecular orbital (MO) to have maximum overlap with the σ*-MO of the single bond undergoing scission, *i.e.* the *p*-MO containing the unpaired electron and the bond undergoing scission are eclipsed.[3]



Scheme 1. Putative ring-opening of 3-(spiro-2'-oxiranyl)bicyclo[2.2.1]heptan-2-yl radicals

The ring-opening of α-oxiranyl radicals has been thoroughly researched[4,5] but not for molecules in which stereoelectronic control might be observed. However, several reports in the literature[6] indicate the possibility of stereoelectronic control in the ring-opening of α-oxiranylcarbinyl radical intermediates. The ring-opening of α-oxiranylcarbinyl radicals normally proceeds by C-O bond cleavage to yield alkoxy radicals rather than C-C bond cleavage to more stable α-alkoxyalkyl radicals, except when vinyl or aryl groups are present as shown.[4,5]

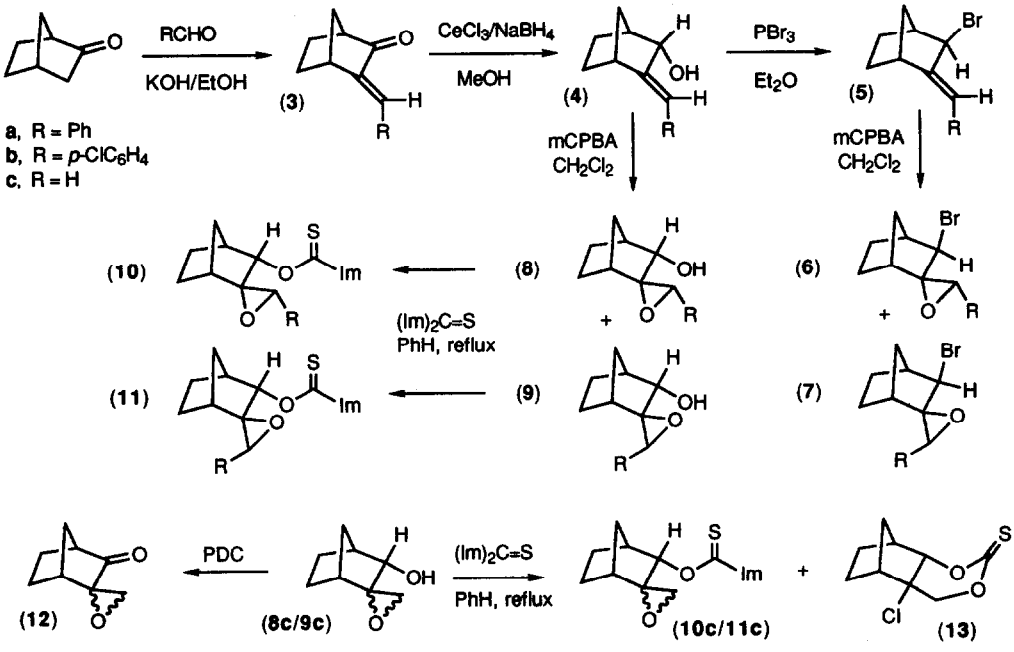


Scheme 2. Preferred TS in the β-scission of α-oxiranyl carbinyl radicals

Jorgensen[7] has suggested that the bond dissociation energy of the C-O bond is lower than the C-C bond except when stabilising groups are present to lower the energy of the C-C bond. The preference for C-O bond cleavage can be explained by reference to the transition states proposed[3,8] for the β-scission of α-cyclopropyl- and cyclobutyl-carbinyl radicals. A polarised TS is favoured in which the α-radical is δ+ and the incipient ring-radical is δ- which would be particularly stabilised for C–O bond cleavage as shown in pathway **a** in Scheme 2.

Synthesis of Radical Precursors

By changing the nature of the substituents on the oxiranes we envisaged that possibly changes in stereo-selectivity would be obtained. Three groups of radical precursors were synthesised which were predicted to yield the required oxiranyl carbinyl radicals (**1**) and (**2**). Scheme 3 shows the synthesis of bromo-, thiocarbonylimidazolyl-, and keto- *endo*- and *exo*-oxiranes. The intermediate α,β-unsaturated ketones (**3**) were reduced with $NaBH_4$ by attack from the less sterically hindered *exo*-face to yield the *endo* alcohols (**4**). The epoxidation of the alkenes (**4**) and (**5**) gave mixtures of *exo* and *endo* isomers. The *exo*-isomer predominated as



Scheme 3. Synthesis of precursors for radical reactions

expected for (**5**) on steric grounds. For the hydroxy-alkenes (**4**), in which the hydroxy group assists delivery of oxygen from the same face of the bicycloheptane, a 1:1 mixture of *endo*- and *exo*-oxiranes (**8**) and (**9**) respectively resulted. The *exo*- and *endo*-isomers were separated by chromatography.

The mixture of hydroxyoxiranes (**8c/9c**) (*endo*:*exo* = 1:4) could not be separated and were converted to the keto-oxiranes (**12**) and -thiocarbonylimidazolides (**10c/11c**). The thiocarbonate (**13**), resulting from HCl catalysed ring-opening of the oxirane and expulsion of imidazole, was formed unless basic conditions were used. Attempts to synthesise the methylene analogues (**6c/7c**) by allylic bromination of norcamphene was unsuccessful owing to the complexity of the bromination product.[9] The allylic alcohol (**4c**) was converted into its 2-*endo*-chloro analogue by reaction with $SOCl_2$ and epoxidised using *m*CPBA.

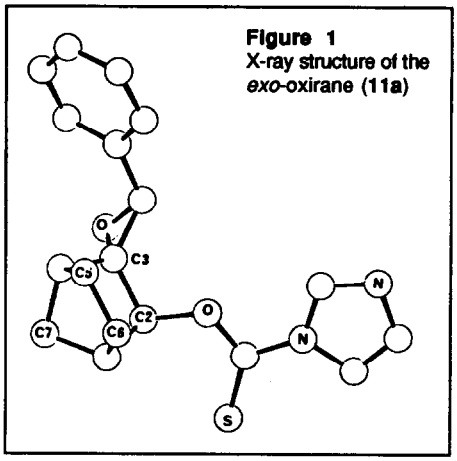
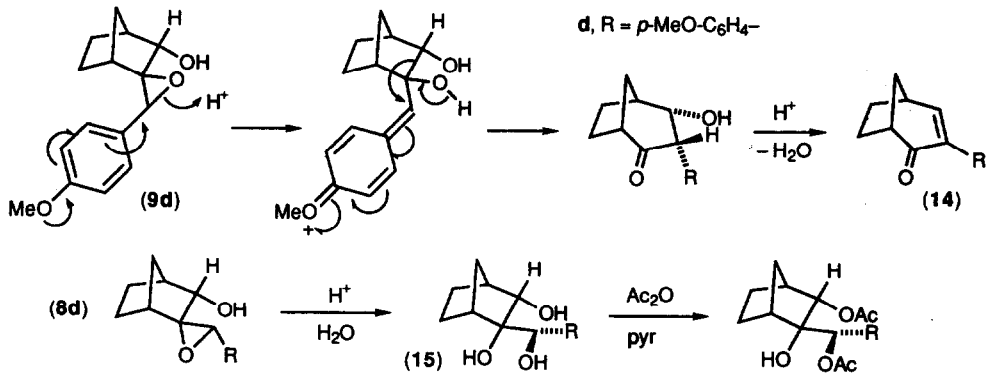


Figure 1
X-ray structure of the *exo*-oxirane (**11a**)

The stereochemistry of the hydroxy and oxiranyl groups in the various isomers was assigned by ^1H NMR spectroscopy and the structure of the *endo*-oxiranyl thiocarbonylimidazolide (**11a**) was confirmed by X-ray crystallography (see Figure 1 and Experimental).

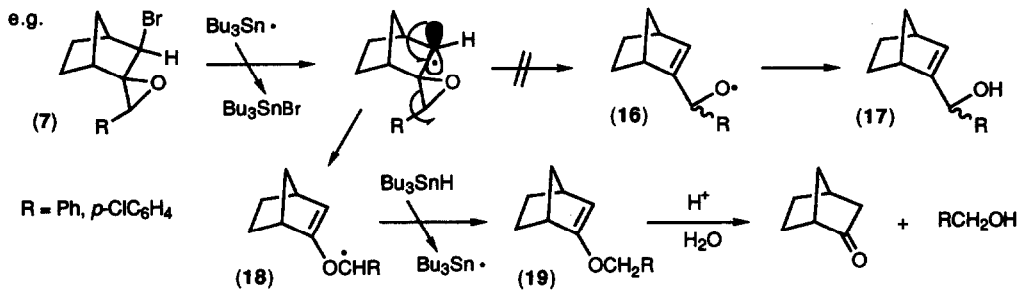
An attempt to prepare the *p*-methoxyphenyl derivatives (**8d/9d**) gave the ring-expanded ketone (**14**) and triol (**15**) (Scheme 4) because of ring-opening during the epoxidation owing to the strong +M effect of the methoxy group. The triol was characterised as its diacetate.



Scheme 4. Rearrangement of the *p*-methoxyphenyloxiranes (**8d**) and (**9d**)

Reaction between bromo-oxiranes and Bu_3SnH

The reduction of the bromo-oxiranes (**6**) and (**7**) with Bu_3SnH yielded norcamphor (35-54%) and benzyl alcohol [34-60% from (**6a/7a**)] and *p*-chlorobenzyl alcohol [38-52% from (**6b/7b**)] respectively [the reaction for (**7**) is shown in Scheme 5]. None of the product (**17**) which would result from C–O bond cleavage was isolated. A sample of (**17a**) was independently prepared for comparison purposes. The results indicate that the oxiranyl-carbinyl intermediate was generated in each case and that the cleavage of the C–C bond results irrespective of the stereochemistry of the oxirane. Clearly the lower energy of the cleavage of the C–C bond with a 3'-aryl substituent on the oxirane overrides energy gains from the preferred line-up of MOs. Only the *exo* oxirane would be predicted to give C–C bond fission under stereoelectronic control. In the *endo* oxirane the C–O bond does not completely eclipse with the 2'-*p* MO of the radical and it appears that stereoelectronic effects are not significant enough to override the preferred C–C bond cleavage. The enol ether (**19**) that results from



Scheme 5. Radical ring-opening of bromo-oxiranes via C–C bond cleavage

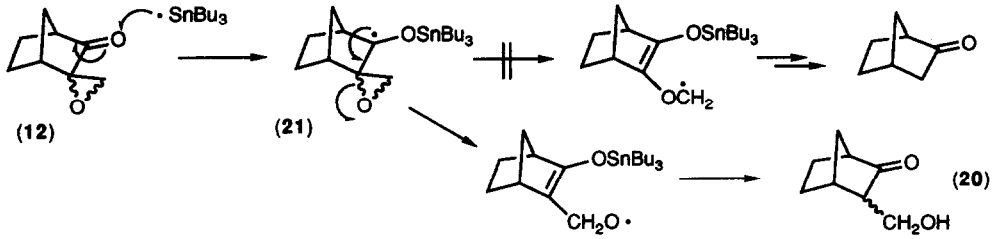
the ring-opening was not isolated. Rapid hydrolysis during work-up gave norcamphor and the respective benzylalcohol.

Our results provide further evidence[4,5] of the importance of the aryl group in directing C–C bond cleavage. An alternative explanation is that C–O bond cleavage does take place in the *endo* oxirane to yield the unstable alkoxy radical (**16**), but that the reaction is reversible. If thermodynamic control is in operation the stable benzyloxy radical (**18**) would be strongly favoured. However, alkoxy radicals are strongly electrophilic[7] and Bu_3SnH a strongly nucleophilic source of hydrogen, and therefore, the intermediate alkoxy radical (**16**) should be rapidly intercepted and reduced by Bu_3SnH to yield (**17**). The rate for reaction[10] between alkoxy radicals and Bu_3Sn• radicals is 2×10^8 $M^{-1}s^{-1}$.

The chloro analogue, 2-*endo*-chlorobicyclo[2.2.1]heptan-3-spiro-2'-oxirane, failed to undergo reaction with Bu_3SnH even with forcing conditions.

Reaction between keto-oxiranes (12) and Bu_3SnH

The keto-oxiranes (**12**) (mixture of *endo* and *exo* isomers) were reduced with Bu_3SnH using the procedure of Hasegawa[11] and Pete[12] to give the hydroxyketone (**20**) (Scheme 6). Although the mechanism[11,12] has not been clearly elucidated, the oxiranyl radicals (**21**) are the probable intermediates, which open by C–O bond cleavage. No norcamphor resulting from C–C bond cleavage was detected. Again the results are in line with those reported,[4,5] *i.e.* C–O bond cleavage is observed if no radical stabilising group is present. Both *endo* and *exo* oxiranes give the same product again, thereby overriding possible stereoelectronic control.

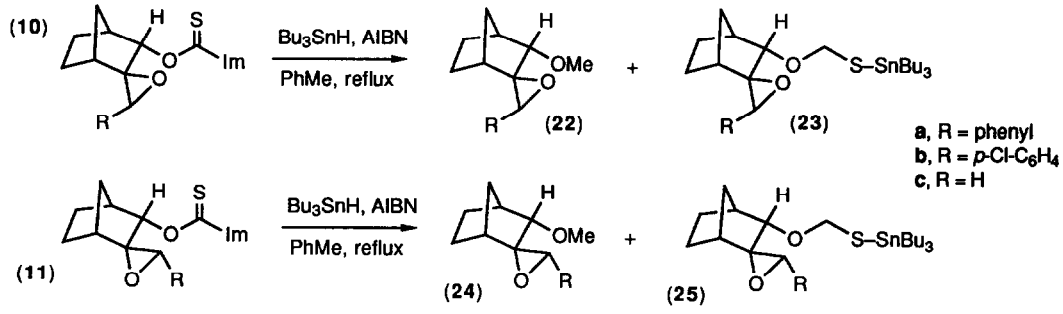


Scheme 6. Radical ring-opening of keto-oxiranes (**12**) *via* C–O bond cleavage

Although stereoelectronic factors were expected to control oxirane ring-opening, other factors appear to be overriding and our examples in previous work[1] and present work have not provided any evidence that stereoelectronic effects are operational, as is observed for cyclopropylcarbinyl radicals. The differences in energy which allow stereoelectronic control in cyclopropylcarbinyl radicals are small, probably smaller than the differences between the strength of C–C and C–O bonds in the respective intermediates.

Reactions between α-oxiranyl thiocarbonyl- imidazolides and Bu_3SnH

The reaction between the *exo*-oxirane (**11a**) and Bu_3SnH (Scheme 7) yielded the methoxy-oxirane (**22a**) (57%), the thioacetal (**23a**), and imidazole (38%), but did not yield any products resulting from ring-opening of the expected intermediate α-oxiranylcarbinyl radical. The use of thiocarbonyl imidazolides for the generation of alkyl radicals is well known,[1,4,13,14] but reduction to methoxy groups has not been reported. The thioacetal (**23a**) was unstable and could not be fully characterised. The *p*-chlorophenyl analogue (**11b**) also gave reduction to the respective methoxy (**22b**) and thioacetal (**23b**) derivatives.



Scheme 7. Reduction of α–oxiranyl-thiocarbonylimidazoles with Bu_3SnH

The methoxyoxirane (**22b**) was synthesised by an alternative route from the alcohol (**4b**) (NaH/MeI followed by epoxidation) and studied by X-ray crystallography (Figure 2) to confirm the structure assigned from NMR spectroscopy. A small amount of the alcohol (**9b**) was isolated, probably resulting from hydrolysis of the thioacetal during work-up. The corresponding phenyl (**11a**) and *p*-chlorophenyl (**11b**) *endo*-oxiranes also gave corresponding products (Scheme 7). Reaction between a mixture of the *endo*- and *exo*-oxiranyl imidazolides, (**10c**) and (**11c**), and Bu_3SnH also failed to give ring-opening but only a mixture of the thioacetals (25%) (**23c**) and (**25c**) were isolated as products.

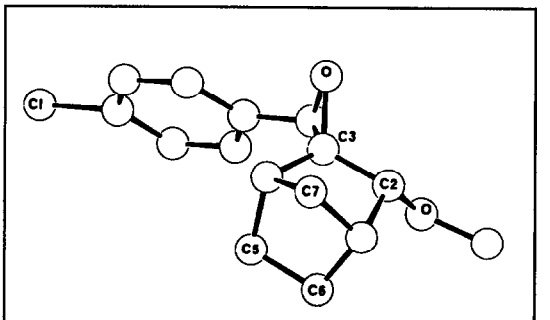
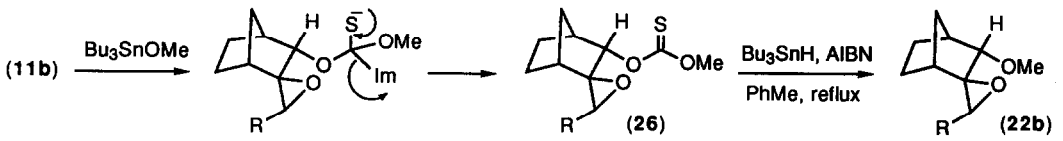


Figure 2. X-ray structure of methoxyoxirane (**22b**)

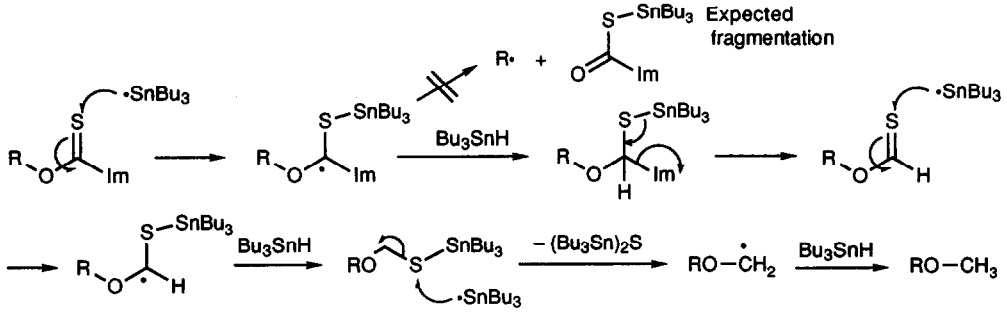
The lack of ring-opening is unusual and we considered that the methoxy products may arise from methanol which is commonly found in commercial Bu_3SnH, but addition of MeOH to reactions gave no difference in yields. Therefore, (**11b**) was allowed to react with Bu_3SnOMe, which may result from reaction between MeOH and Bu_3SnH. The reaction yielded the thiocarbonate (**26**) which was cleanly reduced to the methyl ether (**22b**) with Bu_3SnH (Scheme 8).



Scheme 8. Formation and Bu_3SnH reduction of thiocarbonate (**26**), R = *p*-chlorophenyl

Ten equivalents of Bu_3SnH had been used for most of the reactions at relatively high concentration. When one equivalent of Bu_3SnH was used in the reaction with (**11b**) the ratio of methoxy product (**24b**) to thioacetal (**25b**) changed significantly from 50:50 at 10 equiv. Only the thioacetal was isolated with traces of (**11b**), suggesting that the thioacetal is reduced to the methoxy product by Bu_3SnH. At high dilution of Bu_3SnH only thioacetal was obtained and still no oxirane-opening was observed. The same conditions of reduction (addition of imidazolide to 10 equiv. of Bu_3SnH) gave clean fragmentation in other systems,[1,14] which suggests steric hindrance in these examples. However, molecular models do not show clear-cut steric hindrance. Better results would probably be obtained by syringe-pump addition of dilute Bu_3SnH to a dilute solution of the imidazolide.[14]

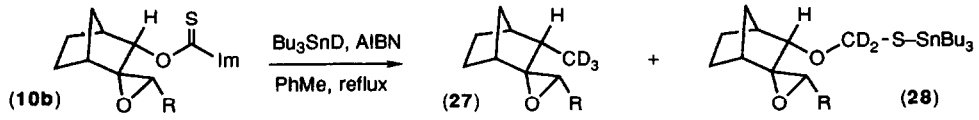
We propose the mechanism shown in Scheme 9, based on the various exceptions to the normal fragmentation of thiocarbonyl imidazolides which have been reported in the literature.[13,14,15-19] Reports[13,14] on the Bu_3SnH reduction of thiocarbonyl imidazolides indicate that if the intermediate radicals are sterically hindered, the dissociation by carbonyl formation is slower than reaction with Bu_3SnH, leading to a variety of products. Thiols are reduced to alkanes *via* Bu_3Sn-SR and therefore reduction of a thiohemiacetal ($ROCH_2SH$) *via* a stable α-alkoxyalkyl radical ($ROCH_2$•) to a methoxy group should be favourable.[13,16] The reduction of thiocarbonyl imidazolides to thiolacetals ($ROCH_2SH$) and then hydrolysis to the alcohol has been reported.[17,18]



Scheme 9. Putative mechanism for the Bu_3SnH reduction of thiocarbonyl imidazolides to methyl ethers

Bu_3Sn• reacts with thioethers to yield alkyl radicals[14] and therefore, reaction with a tributyltin-thioacetal ($ROCH_2S$-$SnBu_3$) to yield $ROCH_2$• should be even more favourable. Further reduction of the α-alkoxymethyl radical with Bu_3SnH would readily yield the methyl ether. Similar precedents are the Bu_3SnH reductions of a thiocarbonate [$(RO)_2C{=}S$] to the acetal [$(RO)_2CH_2$][17] and thioesters to ethers. *e.g.* [ROC(=S)Ph] to ($ROCH_2Ph$).[18,19] The radical formed on Bu_3SnH reduction of thiocarbonyl imidazolides [RO(•CX)S-$SnBu_3$] has sufficient lifetime for other reactions as shown by trapping by cyclisation onto alkenes.[20] The problem of competition between fragmentation and reduction of the initial intermediate radical was identified in the original paper by Barton and McCombie.[18] They also reported[18] isolation of a thioacetal intermediate ($ROCH_2S$-$SnBu_3$) which hydrolysed on silica TLC to yield the corresponding alcohol. Further evidence for the mechanism of formation of alkyl radicals from various thioester species [ROC(=S)X] has been reported.[21]

In order to test the putative mechanism (Scheme 9), the *p*-chlorophenyl oxirane (**10b**) was reduced with Bu_3SnD under the same conditions as for Bu_3SnH. The expected deuteriated products (**27**) and (**28**) were isolated; the ^1H NMR and mass spectra indicated the incorporation of 3D and 2D respectively. These results clearly show that these products arise from Bu_3SnH reduction of the thiocarbonyl imidazolide.



Acknowledgements

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EXPERIMENTAL

General Procedures

IR spectra were obtained using a Pye Unicam PU9516 spectrometer as Nujol mulls unless otherwise stated. ^{1}H-NMR spectra were recorded with a Varian EM360A spectrometer at 60 MHz and a Bruker AC-250 spectrometer at 250 MHz, and ^{13}C-NMR spectra were recorded with a Bruker AC-250 spectrometer at 62.5 MMHz, using $CDCl_3$ as solvent with TMS as an internal standard. Mass spectra were recorded by electron impact with a Kratos MS80 spectrometer. TLC was performed on aluminium plates coated with Merck silica gel 60F254 and compounds were visualised by UV light or iodine vapour. TLC was carried with silica gel or alumina as absorbent. Solvents were purified by standard procedures. Light petroleum is the b.p. 40-60°C fraction. All solutions of products in organic solvents were dried over anhydrous magnesium sulphate. Microanalyses were performed at Brunel University. Tungsten white light fluorescent lamps (2 x 150 W) were used for irradiation.

X-Ray crystallographic data

Positional and temperature parameters, bond lengths, and angles have been deposited with the Cambridge Crystallographic Data Centre, Lensfield Rd., Cambridge, CB2 1EW.

***(E)-endo*-2-[Imidazol-1-yl(thiocarbonyl)oxy]-3'-phenylbicylo[2.2.1]heptan-*endo*-3-spiro-2'-oxirane (11a):** Acicular crystal (0.4 x 0.2 x 0.2 mm) grown from light petroleum. $C_{18}H_{18}N_2O_2S$, orthorhombic, space group Pbca, a = 29.96(2), b = 14.56(2), c = 7.57(2) Å, Z =8, D_c = 1.31 g cm^{-1}, T = 293 K. MoK_α radiation (λ = 0.71069 Å), μ = 1.65 cm^{-1}. Stöe Stadi-2 Weissenberg difractometer, 2765 unique reflections measured of which 1507 had F/σ(F) > 6. Structure solved by direct methods and refined to a final R = 0.0548 (unit weights). All non-H atoms treated anisotropically, H atoms found from difference map and not refined. Maximum shift/error 0.03, $\Delta\rho$ excursions -0.2 to 0.3.

***(E)-endo*-2-methoxy-3'-(4-chlorophenyl)bicylo[2.2.1]heptan-*endo*-3-spiro-2'-oxirane (22b):** crystal (0.6 x 0.6 x 0.3 mm) grown from aqueous MeOH. $C_{15}H_{17}O_2Cl$, monoclinic, space group $P2_1/c$, a = 11.11(1), b = 8.03(1), c = 15.44(2) Å, β = 93.1(5)°, Z = 4, D_c = 1.28 g cm^{-1}, T = 293 K. MoK_α radiation (λ = 0.71069 Å), μ = 2.25 cm^{-1}. Stöe Stadi-2 Weissenberg difractometer, 5223 unique reflections measured of which 1729 had F/σ(F) > 6. Structure solved by direct methods and refined to a final R = 0.0585, R_w = 0.0619. All non-H atoms treated anisotropically, H atoms found from difference map and refined isotropically. Maximum shift/error 0.05, $\Delta\rho$ excursions -0.3 to 0.3.

Synthesis of enones (3) by aldol condensation

(a) *(E)-3-Benzylidenebicyclo[2.2.1]heptan-2-one* (**3a**); *General procedure*: Benzaldehyde (8.5 g, 80 mmol) and potassium hydroxide (4.5 g, 80 mmol) was added to a solution of bicyclo[2.2.1]heptan-2-one (6 g, 54 mmol) in ethanol (100 ml) at room temperature. The mixture was heated to reflux for 1 h until TLC indicated consumption of the starting material. The mixture was cooled, diluted with water, and extracted into diethyl ether. The combined ether extracts were washed with water and brine, dried and the solution was evaporated to dryness to give an oil. The crude oil was purified using column chromatography on TLC silica gel as adsorbent and dichloromethane as eluant to yield the enone (**3a**) (8.8 g, 83%); υ_{max} (neat) 1724 and 1640 cm^{-1}; δ_H (60 MHz) 7.5 (5 H, brs, Ph), 7.2 (1 H, s, C=CH), 3.6 (1 H, brs, H-1), 2.7 (1 H, brs, H-4), and 1.5-2.2 (6 H); *m/z* (E.I.) 198.1045 (M^+, 68%, $C_{14}H_{14}O$ requires 198.1043); λ_{max} (EtOH) 289 (24098) and 224 nm (11463).

(b) *(E)-3-(4-Chlorobenzylidene)bicyclo[2.2.1]heptan-2-one* (**3b**): The crude product was purified using column chromatography with TLC silica gel as adsorbent and dichloromethane:ethyl acetate (13:1) as eluant. Recrystallisation from aqueous methanol gave yellow crystals of the *enone* (**3b**) (71%), m.p. 88-90.5°C;

(Found: C, 72.22; H, 5.61; Cl, 15.26. $C_{14}H_{13}ClO$ requires C, 72.26; H, 5.63; Cl, 15.24%); υ_{max} 1724, 1638, 910, and 734 cm^{-1}; δ_H (90 MHz) 7.22 (4 H, brs, ArH), 6.92 (1 H, s, C=CH), 3.50 (1 H, brs, H-1), and 2.72 (1 H, brs, H-4); *m/z* 234:232 (M^+, 33:100%).

(c) *(E)-3-(4-Methoxybenzylidene)bicyclo[2.2.1]heptan-2-one* (**3d**): The crude product was separated from the starting material by distillation at 0.1 mm Hg. and purified using column chromatography with TLC silica gel as adsorbent and diethyl ether:light petroleum (1:2) as eluant to yield the enone (**3d**) (87%), υ_{max} (neat) 1720, 1636, and 1602 cm^{-1}; δ_H (60 MHz) 6.9-7.5 (4 H, ABq, J = 8 Hz), 7.15 (1 H, s, H-3'), 3.74 (3 H, s, OMe), 3.60 (1 H, brs, H-1) and 2.80 (1 H, brs, H-4); *m/z* (M^+ 228.1150, 100%, $C_{15}H_{18}O_2$ requires 228.1154).

Reduction of enones (3)

(a) *(E)-3-Benzylidenebicyclo-[2.2.1] heptan-endo-2-ol* (**4a**); *General procedure*: Cerous chloride (6.3 g, 17 mmol) was added to a solution of 3-benzylidenebicyclo[2.2.1]heptan-2-one (***4a***) (5.2 g, 26 mmol) in MeOH (150 ml). The mixture was stirred for 5 minutes and $NaBH_4$ (1 g, 26 mmol) was added slowly. The crude product was recrystallised from light petroleum to give light yellow crystals of the *alcohol* (**4a**) (3 g, 58%); m.p. 78-81°C; (Found: C, 83.89 H, 8.11. $C_{14}H_{16}O$ requires C, 83.96, H, 8.05%); υ_{max} 3252 and 1596 cm^{-1}; δ_H (60 MHz) 7.35 (5 H, brs, Ph), 6.40 (1 H, m, C=CH), 4.50 (1 H, brm, J = 2 and 4 Hz, H-2), 3.25 (1 H, brs, H-1), 2.4 (1 H, brs, H-4), and 2.2 (1 H, brs, D_2O exchange, OH); *m/z* (M^+ 200.1201, 100%, $C_{14}H_{16}O$ requires 200.1201).

(b) *(E)-3-(4-Chlorobenzylidene)bicyclo[2.2.1]heptan-endo-2-ol* (**4b**): Recrystallisation (aq. MeOH) of the crude after chromatography gave colourless crystals of the *alcohol* (**4b**) (53%), m.p. 103-106°C; (Found: C, 71.44; H, 6.38. $C_{14}H_{15}ClO$ requires C, 71.64; H, 6.44%); υ_{max} 3280 cm^{-1}; δ_H (90 MHz) 7.1 (4 H, s, Ar-H), 6.2 (1 H, brs, H-3'), 4.4 (1 H, brm, J = 2 and 4 Hz, H-2), 3.1 (1 H, brs, H-1), 2.4 (1 H, brs, H-4) and 1.9 (1 H, s, D_2O exchange, OH); *m/z* 236:234 (M^+, 80:26%).

(c) *3-Methylenebicyclo[2.2.1]heptan-endo-2-ol* (**4c**): The crude oil was purified using column chromatography with TLC silica gel as adsorbent and diethyl ether:light petroleum (1:4) as eluant. The alcohol (**4c**) was obtained as a colourless oil (47%); υ_{max} (neat) 3368 and 1664 cm^{-1}; δ_H (60 MHz) 4.90 (2 H, brs, $C=CH_2$), 4.30 (1 H, m, H-2), 2.70 (1 H, brs, H-4), 2.40 (1 H, brs, H-1), 0.90-2.00 (6 H, m).

(d) *(E)-3-(4-Methoxybenzylidene)bicyclo[2.2.1]heptan-endo-2-ol* (**4d**): Recrystallisation (light petroleum) gave cream crystals of the *alcohol* (**4d**) (43%), m.p. 85-87°C; (Found: C, 77.7; H, 8.13. $C_{15}H_{18}O_2$ requires C, 78.2; H, 7.88%); υ_{max} 3292, 1608, and 1572 cm^{-1}; δ_H (60 MHz) 6.80-7.40 (4 H, ABq, J = 10 Hz), 6.38 (1 H, brs, H-C=CH), 4.50 (1 H, brm, J = 2, 4 Hz, H-2), 3.80 (3 H, s, OMe), 3.30 (1 H, brs, H-1), 2.50 (1 H, brs, H-4) and 1.80 (1 H, s, D_2O exchange, OH); m/z (M^+ 230.1307, 46%, $C_{15}H_{18}O_2$ requires 230.1303).

3-Methylenebicyclo[2.2.1]heptan-2-one (3c)

A hot solution of selenium dioxide (1.6 g, 14 mmol) in dioxan (50 ml) and water (3.3 ml) was added to a hot solution of norcamphene (3 g, 28 mmol) in dioxan (20 ml). The mixture was heated at 60°C for 29 h, diluted with water and extracted into diethyl ether. The ether was washed with water, dried and the solution evaporated to dryness to yield a crude product of the alcohol (**4c**) (2.2 g, 65%). The alcohol was oxidised with pyridinium dichromate and the crude product was purified using column chromatography (TLC silica gel) with CH_2Cl_2 as eluant to yield the ketone (**3c**) as a yellow oil (1 g, 46%); υ_{max} (neat) 1740 and 1640 cm^{-1}; δ_H (60 MHz) 5.70 (1 H, brs, C=CH), 5.20 (1 H, brs, C=CH), 3.20 (1 H, brs, H-1), and 2.70 (1 H, brs, H-4).

Synthesis of bromoalkenes (5)

(a) *(E)-3-Benzylidene-exo-2-bromobicyclo[2.2.1]heptane* (**5a**); *General procedure*: Phosphorous tribromide (2.8 g, 11 mmol) was slowly added to a solution of allylic alcohol (**4a**) (2 g, 10 mmol) in dry diethyl ether (100 ml) at room temperature. The mixture was stirred overnight, diluted with Et_2O, poured onto ice, and the layers separated. The organic layer was washed with water, dried, and the solution evaporated to dryness to yield a crude oil the bromoalkene (**5a**) (2.0 g, 76%) which was reacted without further purification; υ_{max} (neat)

2940 and 1600 cm^{-1}; δ_H (60 MHz) 7.30 (5 H, s, Ph), 6.60 (1 H, s, C=CH), 4.60 (1 H, m, J = 1.8, 3 Hz, H-2), 3.30 (1 H, brs, H-4) and 2.60 (1 H, brs, H-1).

(b) *(E)-exo-2-Bromo-3-(4-chlorobenzylidenebicyclo[2.2.1]heptane* (**5b**); Recrystallisation (diethyl ether/ EtOH) gave colourless crystals of the bromoalkene (**5b**) (40%), m.p. 85-88°C; (Found: C, 56.48; H, 4.72; Br, 26.62. $C_{14}H_{14}BrCl$ requires C, 56.60; H, 4.79; Br, 26.85%); δ_H (60 MHz) 7.40 (4 H, s), 6.70 (1 H, brs, H-3'), 4.60 (1 H, m, J = 1.8, 3 Hz, H-2), 3.30 (1 H, brs, H-4) and 2.60 (1 H, brs, H-1); *m/z* (M^+ 300/298/296).

Epoxidation reactions

(a) *(E)-endo-2-Hydroxy-3'-phenylbicyclo[2.2.1]heptan-endo-3-spiro-2'-oxirane* (**8a**); *General procedure*: *m*-Chloroperbenzoic acid (1.7 g, 10 mmol) was added to a solution of the alcohol (**4a**) (1 g, 5 mmol) in CH_2Cl_2 (40 ml) at room temperature. The mixture was stirred with solid sodium hydrogencarbonate for 4 h. The crude residue was separated using preparative TLC with silica gel as adsorbent and Et_2O:light petroleum (1:1) as eluant. Two products were isolated in a 50:50 mixture.

The less polar product was recrystallised (aq. MeOH) to give colourless crystals of *the oxirane* (**8a**) (0.34 g, 32%); m.p. 89-91°C; (Found: C, 77.89; H, 7.59. $C_{14}H_{16}O_2$ requires C, 77.75, H, 7.46%); υ_{max} 3240 and 1108 cm^{-1}; δ_H (250 MHz) 7.20-7.40 (5 H, m, Ph), 4.02 (1 H, d, J = 2.7 Hz, H-2), 4.00 (1 H, s, H-3'), 2.51 (1 H, brs, H-1), 2.41 (1 H, brs, D_20 exchange, OH), and 1.90 (1 H, brs, H-4); δ_C (250 MHz) 135.62, 128.24, 127.86, 126.04, 72.34 (C-3), 71.48 (C-2), 65.01 (C-3'), 41.82 (C-1), 35.94 (C-4), 32.66 (C-5), 24.41 (C-7), 12.69 (C-6); *m/z* 216.1150 (M^+, 7.2%, $C_{14}H_{16}O_2$ requires 216.1153).

(E)-endo-2-Hydroxy-3'-phenylbicyclo[2.2.1]heptan-exo-3-spiro-2'-oxirane (**9a**): The more polar product was recrystallised (aq. MeOH) to give colourless crystals of the *oxirane* (**9a**) (0.4 g, 36%); m.p. 91.5-93°C; (Found: C, 77.98; H, 7.60. $C_{14}H_{16}O_2$ requires C, 77.75; H, 7.46%); υ_{max} 3400 and 1094 cm^{-1}; δ_H (250 MHz) 7.2-7.3 (5 H, m, Ph), 4.23 (1 H, s, H-3'), 4.08 (1 H, d, J = 3 Hz, H-2), 2.47 (1 H, brs, H-1) and 1.99 (1 H, brs, H-4); δ_C (250 MHz) 136.51, 128.08, 127.41, 125.96, 77.95 (C-2), 76.36 (C-3), 58.89 (C-3'), 42.42 (C-1), 39.04 (C-4), 34.14 (C-7), 24.15 (C-5), and 19.05 (C-6); *m/z* 216.1150 (M^+, 9.6%, $C_{14}H_{16}O_2$ requires 216.1143).

(b) *(E)-3'-(4-Chlorophenyl)-endo-2-hydroxybicyclo[2.2.1]heptan-endo-3-spiro-2'-oxirane* (**8b**): (23%), m.p. 85-88°C; (Found: C, 67.01; H, 6.09. $C_{14}H_{15}ClO_2$ requires C, 67.07; H, 6.03%); υ_{max} 3376 cm^{-1}; δ_H (60 MHz) 7.10-7.40 (4 H, ABq, J = 10 Hz), 4.10 (1 H, d, J = 4 Hz, H-2), 3.98 (1 H, s, H-3'), 2.50 (2 H, brs, H-1, D_20 exchange OH), 1.90 (1 H, brs, H-4); *m/z* M^+ 252:250.

(E)-3'-(4-Chlorophenyl)bicycloendo-2-hydroxy-[2.2.1]heptan-exo-3-spiro-2'-oxirane (**9b**): (30%), m.p. 140-144°C; (Found: C, 66.93; H, 6.03. $C_{14}H_{15}ClO_2$ requires C, 67.07; H, 6.03%); υ_{max} 3404 cm^{-1}; δ_H (60 MHz) 7.33 (4 H, s), 4.23 (1 H, s, H-3'), 4.00 (1 H, d, J = 4 Hz, H-2), 3.40 (1 H, m, D_20 exchange, OH), 2.45 (1 H, brs, H-1) and 1.90 (1 H, brs, H-4); *m/z* M^+ 252:250.

(c) *endo-2-Hydroxybicyclo[2.2.1]heptan-exo/endo-3-spiro-2'-oxirane* (**8c/9c**): A mixture of isomers was obtained which could not be separated by chromatography. ^1H NMR spectroscopy showed a 4:1 mixture of the *endo/exo*-epoxides (**8c/9c**) (45%); υ_{max} (neat) 3436 cm^{-1}; δ_H (90 MHz) 3.90 (1 H, d, J = 4 Hz, H-2), 2.90-3.20 (2 H, ABq, J = 4.5 Hz, H-3'), 2.50 (1 H, brs, H-1) and 2.05 (1 H, brs, H-4); *m/z* (M^+ 140.0824, 3%, $C_8H_{12}O_2$ requires 140.082).

(d) *Attempted synthesis of hydroxyoxiranes* (**8d/9d**): The less polar product obtained was recrystallised (aq.MeOH) to give colourless crystals of *3-(4-methoxyphenyl)bicyclo[3.2.1]oct-3-en-2-one* (**14**) (4%); m.p. 53-55°C; (Found: C, 78.76; H, 6.94. $C_{15}H_{16}O_2$ requires C, 78.91; H, 7.06%); υ_{max} 1670, 1600, and 1510 cm^{-1}; δ_H (60 MHz) 6.80-7.40 (4 H, ABq, J = 8 Hz), 7.30 (1 H, m, H-4), 3.80 (3 H, s, OMe), and 2.83-3.10 (2 H, m, H-5, H-1); *m/z* (M^+ 228.1150, 100%, $C_{15}H_{16}O_2$ requires 228.1153). The more polar product was recrystallised from diethyl ether to give colourless crystals of *exo-3-[hydroxy(4-methoxybenzyl)]bicyclo[2.2.1] -heptan-endo-2,3-diol* (**15**) (6%), m.p. 149-151°C; (Found: C, 67.93; H, 7.28. $C_{15}H_{20}O_4$ requires C, 68.16; H, 7.63%); υ_{max} 3428 cm^{-1}; δ_H (60 MHz) 6.80-7.50 (4 H, ABq, J = 8 Hz), 4.95 (1 H, brs, H-3'), 4.30 (1 H, brs, D_2O exchange, OH), 3.92 (1 H, d, J = 4.5 Hz, H-2), 3.80 (3 H, s, OMe), 3.38 (1 H, s, D_2O exchange, OH), 3.00 (1 H, brs, D_2O exchange, OH), 2.40 (1 H, brs, H-1) and 1.95 (1 H, brs, H-4); *m/z* (M^+ 264.1362,

$C_{15}H_{20}O_4$ requires 264.1362. The triol was acetylated with acetic anhydride/pyridine, purified by preparative TLC with silica gel as adsorbent and ethyl acetate:light petroleum (1:1) as eluant. Recrystallisation (Et_2O/light petroleum) gave colourless crystals of *exo-3-[acetoxy(4-methoxybenzyl)]-endo-2-acetoxybicyclo [2.2.1]heptan-endo-3-ol* (16%); m.p. 152-155°C; (Found: C, 65.61; H, 6.97. $C_{19}H_{24}O_6$ requires C, 65.50; H, 6.94%); υ_{max} 3520, 1740, and 1240 cm^{-1}; δ_H (60 MHz) 6.80-7.65 (4 H, ABq, J = 9 Hz), 5.92 (1 H, brs, H-3'), 4.90 (1 H, d, J = 4 Hz, H-2), 3.82 (3 H, s, OMe), 2.80 (1 H, brs, D_2O exchange, OH), 2.07 (3 H, s, OAc), 2.00 (3 H, s, OAc), and 2.1-1.9 (2 H, brs, H-1,4); *m/z* (M^+ 348.1573, 2%, $C_{19}H_{24}O_6$ requires 348.1574).

(e) *(E)-exo-2-Bromo-3'-phenylbicyclo[2.2.1]heptan-endo-3-spiro-2'-oxirane* (**6a**): The less polar isomer was isolated as a colourless oil of the *bromo-oxirane* (**6a**) (31%); (Found: C, 60.18; H, 5.41. $C_{14}H_{15}BrO$ requires C, 60.23; H, 5.42%); δ_H (60 MHz) 7.32 (5 H, s, ArH), 4.40 (1 H, s, H-3'), 3.95 (1 H, d, J = 4 Hz, H-2), 2.70 (1 H, brs, H-4) and 2.00 (1 H, brs, H-1); *m/z* M^+ 280/278.

(E)-exo-2-Bromo-3'-phenylbicyclo[2.2.1]heptan-exo-3-spiro-2'-oxirane (**7a**): The more polar isomer was isolated as a colourless oil of the *bromo-oxirane* (**7a**) (19%); (Found: C, 60.46; H, 5.53. $C_{14}H_{15}BrO$ requires C, 60.23; H, 5.42%); δ_H (60 MHz) 7.40 (5 H, s, ArH), 4.40 (1 H, s, H-3'), 4.30 (1 H, d, J = 4 Hz, H-2), 2.60 (1 H, brs, H-4), and 2.00 (1 H, brs, H-1); *m/z* M^+ 280/278.

(f) *(E)-exo-2-Bromo-3'-(4-chlorophenyl)bicyclo[2.2.1]heptan-endo-3-spiro-2'-oxirane* (**6b**): The less polar product was recrystallised (aq. EtOH) to give colourless crystals of the *bromo-oxirane* (**6b**) (20%); m.p. 68-70°C; (Found: C, 53.70; H, 4.48. $C_{14}H_{14}BrClO$ requires C, 53.62; H, 4.50%); δ_H (250 MHz) 7.20-7.40 (4 H, ABq, J = 5.9 Hz, ArH), 4.36 (1 H, s, H-3'), 3.67 (1 H, d, J = 1.9 Hz, H-2), 2.65 (1 H, brs, H-4), and 2.10 (1 H, brs, H-1); δ_C 134.73, 133.72, 128.56, 127.40, 77.75 (C-3), 67.60 (C-2), 58.47 (C-3'), 47.20 (C-4), 37.81 (C-1), 36.11 (C-7), 27.43 (C-5), and 23.54 (C-6); *m/z* M^+ 316/314/312.

(E)-exo-2-Bromo-3'-(4-chlorophenyl)bicyclo[2.2.1]heptan-exo-3-spiro-2'-oxirane (**7b**): The more polar isomer was recrystallised (aq. EtOH) to give colourless crystals of the *bromo-oxirane* (**7b**) (11%); m.p. 86-90°C; (Found: C, 53.78; H, 4.51. $C_{14}H_{14}BrClO$ requires C, 53.62; H, 4.50%); δ_H (250 MHz) 7.20-7.34 (4 H, m, ArH), 4.30 (1 H, s, H-3'), 4.20 (1 H, d, J = 2 Hz, H-2), 2.64 (1 H, brs, H-4), and 1.97 (1 H, brs, H-1); δ_C (250 MHz) 134.62, 133.53, 128.46, 127.25, 76.35 (C-3), 63.61 (C-2), 58.6 (C-8), 43.92 (C-8), 38.73 (C-1), 35.68 (C-7), 23.5 (C-5) and 23.68 (C-6); *m/z* M^+ 316/314/312.

Synthesis of oxiranylthiocarbonylimidazolides

(a) *(E)-endo-2-[Imidazol-1-yl(thiocarbonyl)oxy]-3'-phenylbicyclo[2.2.1]heptan-endo-3-spiro-2'-oxirane* (**10a**); *General procedure*: A solution of the oxiranylalcohol (**8a**) (0.4 g, 1.8 mmol) and *N,N'*-thiocarbonyl diimidazole (0.7 g, 4 mmol) in benzene (30 ml) was heated to reflux under oxygen-free nitrogen until the reaction was complete as indicated by TLC (*ca.* 3 h). The reaction solution was evaporated to dryness and the residue dissolved in CH_2Cl_2. The CH_2Cl_2 solution was washed with water, hydrochloric acid (1 M), 5% aqueous $NaHCO_3$ solution, and water, dried and evaporated to dryness. The residue was recrystallised (light petroleum, b.p.40-60°C) to give cream crystals of the *thiocarbonylimidazolide* (**10a**) (0.4 g, 63%), m.p. 117.5-119°C; (Found: C, 66.25; H, 5.61; N, 8.59. $C_{18}H_{18}N_2O_2S$ requires C, 66.03; H, 5.85; N, 8.56%); υ_{max} 3168, 1150, 1040, and 1010 cm^{-1}; δ_H (60 MHz) 8.50 (1 H, brs, H-Im), 7.70 (1 H, brs, H-Im), 7.40 (5 H, brs, Ph), 7.10 (1 H, brs, H-Im), 5.90 (1 H, d, J = 4 Hz, H-2), 4.20 (1 H, s, H-3'), and 2.90 (1 H, brs, H-1); *m/z* (M^++1 327.1167, 18%, $C_{18}H_{19}N_2O_2S$ requires 327.1132).

(b) *(E)-3'-(4-Chlorophenyl)-endo-2-[imidazol-1-yl(thiocarbonyl)oxy]-bicyclo[2.2.1]heptan-endo-3-spiro-2'-oxirane* (**10b**): The crude product was purified using column chromatography with TLC silica gel as adsorbent and diethyl ether:light petroleum (1:4) as eluant to yield a colourless oil of the thiocarbonylimidazolide (**10b**) (69%). υ_{max} ($CDCl_3$) 3176, 1450, 1380, 1320, and 1280 cm^{-1}; δ_H (60 MHz) 8.50 (1 H, brs, H-Im), 7.70 (1 H, brs, H-Im), 7.20-7.50 (4 H, ABq, J = 10 Hz, ArH), 7.32 (1 H, brs, H-Im), 5.90-6.00 (1 H, d, J = 4.5 Hz, H-2) 4.35 (1 H, s, H-3'), and 2.90 (1 H, brs, H-1), 1.9 (1 H, brs, H-4); *m/z* M^+ 362:360.

(c) *(E)-endo-2-[Imidazol-1-yl(thiocarbonyl)oxy]-3'-phenylbicyclo[2.2.1]heptan-exo-3-spiro-2'-oxirane* (**11a**): Cream crystals (30%), m.p. 150-152°C (Et_2O/light petroleum); (Found: C, 66.14; H, 5.67; N, 8.54. $C_{18}H_{18}N_2O_2S$ requires C, 66.03; H, 5.85; N, 8.56%); υ_{max} 3168, 1150, 1040, and 1012 cm^{-1}; δ_H (60 MHz)

8.50 (1 H, brs, H-Im), 7.70 (1 H, brs, H-Im), 7.40 (5 H, s, Ph), 7.20 (1 H, brs, H-Im), 5.70 (1 H, d, J = 4 Hz, H-2), 4.20 (1 H, s, H-3'), 3.10 (1 H, brs, H-1), and 2.10 (1 H, brs, H-4); *m/z* M^++1 327.

(d) *(E)-3'-(4-Chlorophenyl)-endo-2-[imidazol-1-yl(thiocarbonyl)oxy]-bicyclo[2.2.1]heptan-exo-3-spiro-2'-oxirane* (**11b**): Colourless crystals (69%); m.p. 143-145°C; (Found: C, 59.64; H, 4.72; N, 7.68. $C_{18}H_{17}ClN_2O_2S$ requires C, 59.75; H, 4.73; N, 7.74%); υ_{max} 3176, 1148, and 1045 cm^{-1}; δ_H (60 MHz) 8.40 (1 H, brs, H-Im), 7.70 (1 H, brs, H-Im), 7.30 (4 H, s, ArH), 7.10 (1 H, brs, H-Im), 5.60 (1 H, d, J = 4 Hz, H-2), 4.10 (1 H, s, H-3'), 3.00 (1 H, brs, H-1), and 2.00 (1 H, brs, H-4); *m/z* M^+ 362:360 (1:3).

(e)*endo-2-[Imidazol-1-yl(thiocarbonyl)oxy]bicyclo[2.2.1]heptan-exo/endo-3-spiro-2'-oxirane* (**10c/11c**): The more polar product was isolated as colourless oil of *exo* and *endo* isomers (**10c/11c**) (10%) which could not be separated; (Found: C, 57.86; H, 5.71; N, 10.93. $C_{12}H_{14}N_2O_2S$ requires C, 57.58; H, 5.60; N, 11.20%); υ_{max} (neat) 3176, 1450, 1380, 1320, 1280, and 970 cm^{-1}; δ_H (60 MHz) 8.30 (1 H, brs, H-Im), 7.60 (1 H, brs, H-Im), 7.10 (1 H, brs, H-Im), 5.60 (1 H, d, J = 4 Hz, H-2), 3.10 (1 H, brs, H-4) and 2.98 (2 H, ABq, J = 4.5 Hz, H-3') 2.00 (1 H, brs, H-1); *m/z* M^+ (250.0776, 20%, $C_{12}H_{14}N_2O_2S$ requires 250.0773).

Cyclic thiocarbonate ether (**13**): The less polar product was recrystallised (Et_2O) to give colourless crystals of (**13**) (4%), m.p. 110-112.5°C; (Found: C, 49.34; H, 5.01; S, 14.40. $C_9H_{12}ClO_2S$ requires C, 49.42; H, 5.08; S, 14.63%); υ_{max}(CCl_4) 1540, 1462, 1380, and 1366 cm^{-1}; δ_H (250 MHz) 4.90 (1 H, d, J = 4.8 Hz, H-2), 3.53-3.99 (2 H, ABq, J = 12.6 Hz, H-3'), 2.80 (1 H, brs, H-4), and 2.52 (1 H, brs, H-1); δ_C 191.64 (C=S), 95.18 (C-3), 86.40 (C-2), 44.03 (C-4), 40.63 (C-1), 35.66 (C-7), 22.56 (C-5) and 20.02 (C-6); *m/z* (M^+ 220.014/218.017, 17:49%, $C_9H_{12}ClO_2S$ requires 220.013/218.013).

Bicyclo[2.2.1]heptan-2-one-3-spiro-2'-oxirane (12)

The hydroxyoxirane (**8c**) (0.6 g, 4.3 mmol) in CH_2Cl_2 (50 ml) was oxidised with PDC (3 g, 8 mmol). Standard work-up gave a 4:1 mixture of *exo* and *endo* (**12**) as a colourless oil (0.24 g, 41%); υ_{max} (neat) 1754 cm^{-1}; δ_H (250 MHz) 2.80-3.14 (2 H, ABq, J = 5.6 Hz, H-3'), 2.80 (1 H, brs, H-1), and 2.41 (1 H, brs, H-4); δ_C 213.79 (C-2), 63.57 (C-3), 49.31 (C-3'), 48.97 (C-1), 40.10 (C-4), 35.97 (C-7), 25.10 (C-5). and 23.79 (C-6); *m/z* (M^+ 138.0681, 4%, $C_8H_{10}O_2$ requires 138.0714).

Bu_3SnH reductions

General procedure: The substrate (*ca.* 0.5 g) and AIBN (0.1 equiv.) in toluene (2-6 ml) was added to a refluxing solution of Bu_3SnH (10 equiv.) in toluene (5-10 ml) under oxygen-free nitrogen over 10-20 minutes. The reactions were followed by TLC (normally *ca.* 1 h). After cooling the solvent was removed *in vacuo*. The crude residue was purified by short column chromatography using TLC silica gel as adsorbent and light petroleum as eluant to remove most of the Bu_3SnH. The column was then eluted with diethyl ether. The fractions were further purified using preparative TLC with silica gel as absorbent, except for thioacetals where alumina was used as adsorbent, and diethyl ether:light petroleum as eluant.

(a) *Bu_3SnH reductions of (E)-exo-2-bromo-3'-arylbicyclo[2.2.1]heptan-endo/exo-3-spiro-2'-oxiranes*: The *endo-bromo-oxirane* (**6a**) gave two products. The less polar product isolated was bicyclo[2.2.1]heptan-2-one (norcamphor) (35%); υ_{max} ($CDCl_3$) 1745 cm^{-1}; TLC and ^1H NMR and IR spectra were identical to authentic material. The 2,4-dinitrophenylhydrazone derivative had the correct m.p. (127-129°C). The more polar product isolated was benzylalcohol (60%). The m.p. and IR and ^1H NMR spectra and the 3,5-dinitrobenzoate derivative (m.p. 109-110°C) were identical to authentic material. The *exo*-bromo-oxirane (**7a**) gave similar results. The *endo*-bromo-oxirane (**6b**) yielded [2.2.1]bicycloheptan-2-one (45%) and colourless crystals of 4-chlorobenzyl alcohol (23%), m.p. 71-73°C, which were identified as above. The *exo*-bromo-oxirane (**7b**) gave similar results.

(b) *Bu_3SnH reduction of bicyclo[2.2.1]heptan-2-one-3-spiro-2'-oxirane* (**12**): The reaction was refluxed for 6 h. Work-up gave a colourless oil of 3-hydroxymethylbicyclo[2.2.1]heptan-2-one (**20**) (72%) as the only product; υ_{max} (neat) 3428 and 1730 cm^{-1}; δ_H (250 MHz) 3.60-3.88 (2 H, ABX, J = 7.4 Hz, CH_2OH), 2.72 (1 H, brs, H-1), 2.70 (1 H, d, J = 5 Hz, H-4), 2.39 (2 H, m, H-3 and OH, lost on D_20 exchange), and 1.50-1.88

(6 H); δ_C (250 MHz) 219.96 (C-2), 60.74 (CH_2OH), 55.32 (C-1), 50.45 (C-3), 37.95 (C-4), 37.95 (C-7), 25.39 (C-5), and 21.80 (C-6); *m/z* (M^+ 140.0837, 4%, $C_8H_{12}O_2$ requires 140.0846).

(c) *Bu_3SnH reduction of (E)-endo-2-[imidazol-1-yl(thiocarbonyl)oxy]-3'-phenylbicyclo[2.2.1]heptan-exo- 3-spiro-2'-oxirane* (**11a**): The less polar fraction yielded a colourless oil of the thioacetal (**23a**) (8%) δ_H (250 MHz) 7.26-7.34 (5 H, m, ArH), 4.70-4.91 (2 H, ABq, J = 6.9 Hz, OCH_2S), 4.13 (1 H, d, J = 3 Hz, H-2), 4.14 (1 H, s, H-3'), 2.62 (1 H, brs, H-4), and 1.96 (1 H, brs, H-1), and 0.80-1.80 (other H). The more polar fraction was recrystallised (aq. MeOH) to give colourless crystals of *methoxyoxirane* (**22a**) (57%); m.p. 47-48.5°C; (Found: C, 73.45; H, 7.14. $C_{15}H_{18}O_3$ requires C, 73.15; H, 7.37%); υ_{max} 1106 cm^{-1}; δ_H (250 MHz) 7.20-7.36 (5 H, m, ArH), 4.22 (1 H, s, H-3'), 3.58 (1 H, d, J = 2.8 Hz, H-2), 3.32 (3 H, s, OMe), 2.63 (1 H, brs, H-4) and 1.94 (1 H, brs, H-1); δ_C (250 MHz) 136.77, 128.1, 127.4, 126.13, 86.4 (C-2), 75.4 (C-3), 58.89 (C-4), 57.28 (C-1), 38.59 (OMe), 33.92 (C-7), 24.24 (C-5) and 19.1 (C-6); *m/z* (M^+ 230.1298, 55%, $C_{15}H_{18}O_2$ requires 230.1298). Further elution with methanol gave imidazole (38%), m.p. 87-89°C (from Et_2O). The TLC and IR and ^1H NMR spectra were identical to those of authentic imidazole.

(d) *Bu_3SnH reduction of (E)-endo-2-[imidazol-1-yl(thiocarbonyl)oxy]-3'-phenylbicyclo[2.2.1]heptan-endo-3-spiro-2'-oxirane* (**10a**): Analysis of the crude by ^1H NMR spectroscopy showed a 1:1 mixture of the methoxyoxirane (**24a**) and the thioacetal (**25a**). The thioacetal was lost during further purification; δ_H (60 MHz) 7.30 (5 H, s, ArH), 4.95 (2 H, s, OCH_2S), 4.35 (1 H, d, J = 4 Hz, H-2), 4.0 (1 H, s, H-3'), 2.60 (1 H, brs, H-4), and 1.95 (1 H, brs, H-1). *Methoxyoxirane* (**24a**): (30%); m.p. 44-46.5°C (from aq. MeOH); (Found: C, 78.04; H, 7.93. $C_{15}H_{18}O_2$ requires C, 78.23; H, 7.88%); υ_{max} 1110 cm^{-1}; δ_H (250 MHz) 7.20-7.37 (5 H, m, ArH), 3.96 (1 H, s, H-3'), 3.70 (1 H, d, J = 2.8 Hz, H-2), 3.37 (3 H, s, OMe) and 2.59 (1 H, brs, H-4) 1.75 (1 H, brs, H-1); δ_C (250 MHz) 136.47, 128.1, 127.48, 126.1, 80.59 (C-2), 71.1 (C-3), 64.47 (C-3'), 57.56 (OMe), 39.34 (C-4), 36.63 (C-1), 32.72 (C-7), 23.86 (C-5), and 19.5 (C-6); *m/z* (M^+ 230.1307, 50%, $C_{15}H_{18}O_2$ requires 230.1310). Further elution with methanol gave imidazole (60%).

(e) *Bu_3SnH reduction of (E)-3'-(4-chlorophenyl)-endo-2-[imidazol-1-yl(thiocarbonyl)oxy]bicyclo-[2.2.1]heptan-exo-3-spiro-2'-oxirane* (**11b**): Thioacetal (**23b**) (33%); δ_H (60 MHz) 7.30 (4 H, s, ArH), 4.6-5.0 (2 H, ABq, J = 10 Hz, OCH_2S), 4.25 (1 H, d, J = 4 Hz, H-2), 4.14 (1 H, s, H-3'), 2.65 (1 H, brs, H-4), and 1.97 (1 H, brs, H-1). *Methoxyoxirane* (**22b**) (48%); m.p. 63-65°C (colourless crystals from aq. MeOH); (Found: C, 67.99; H, 6.61. $C_{15}H_{17}ClO_2$ requires C, 68.05; H, 6.47%); υ_{max} 1106 cm^{-1}; δ_H (250 MHz) 7.28 (4 H, m, ArH), 4.18 (1 H, s, H-3'), 3.56 (1 H, d, J = 2.9 Hz, H-2), 3.31 (3 H, s, OMe), 2.63 (1 H, brs, H-4) and 1.90 (1 H, brs, H-1); δ_C (250 MHz) 135.34, 133.1, 128.25, 127.43, 86.16 (C-2), 75.49 (C-3), 58.24 (C-3'), 57.18 (OMe), 38.61 (C-4), 38.5 (C-1), 33.83 (C-7), 24.18 (C-5), and 18.97 (C-6); *m/z* M^+ 266/264. A more polar fraction was recrystallised (aq. MeOH) to give colourless crystals of *exo*-oxiranylalcohol (**9b**) (6%). The m.p., TLC, and ^1H NMR and IR spectra were identical to the synthetic material. Further elution gave a small amount of imidazole.

(f) *Bu_3SnH reduction of (E)-3'-(4-chlorophenyl)endo-2-[imidazol-1-yl(thiocarbonyl)oxy]bicyclo[2.2.1]-heptan-endo-3-spiro-2'-oxirane* (**10b**): Thioacetal (**25b**) (20%); δ_H (250 MHz) 7.10-7.33 (4 H, ABq, J = 5.9 Hz, ArH), 4.80-5.00 (2 H, ABq, J = 8 Hz, OCH_2S), 4.17 (1 H, d, J = 2.8 Hz, H-2), 3.99 (1 H, s, H-3'), 2.54 (1 H, brs, H-4), and 1.70 (1 H, brs, H-1). *Methoxyoxirane* (**24b**) (35%); m.p. 47-50°C (colourless crystals from aq. MeOH); (Found: C, 68.10; H, 6.35. $C_{16}H_{17}ClO_2$ requires C, 68.05; H, 6.47%); δ_H (250 MHz) 7.20-7.33 (4 H, ABq, J = 5.8 Hz, ArH), 3.93 (1 H, s, H-3'), 3.68 (1 H, d, J = 2.8 Hz, H-2), 3.36 (3 H, s, OMe), 2.59 (1 H, brs, H-4), and 1.69 (1 H, brs, H-1); δ_C (250 MHz) 135.02, 133.31, 128.34, 127.42, 80.47 (C-2), 71.25 (C-3), 63.86 (C-3'), 57.57 (OMe), 39.30 (C-4), 36.57 (C-1), 32.67 (C-7), 23.86 (C-5) and 19.44 (C-6); m/z M^+ 266/264.

(g) *Bu_3SnH reduction of endo-2-[imidazol-1-yl(thiocarbonyl)oxy]bicyclo[2.2.1]heptan-exo/endo-3-spiro-2'-oxirane* (**10c/11c**): Only the thioacetals (**23c/25c**) were isolated as a colourless oil (25%); δ_H (250 MHz) 4.60-4.82 (2 H, ABq. J = 9.9 Hz, OCH_2S), 4.15 (1 H, d, J = 2.8 Hz, H-2), 2.60-2.91 (2 H, ABq, J = 5 Hz, H-3'), 2.52 (1 H, brs, H-4), and 1.79 (1 H, brs, H-1).

(h) *Bu_3SnH reduction of (E)-endo-2-[methoxy(thiocarbonyl)oxy]-3'-(4-chlorophenyl)bicyclo[2.2.1]-heptan-exo-3-spiro-2'-oxirane* (**26**): Colourless crystals of methoxyoxirane (**22b**) (14%) were obtained as the sole product. The TLC and ^1H NMR and IR spectra were identical to those of previously synthesised (**22b**).

The thiocarbonate (**26**) was prepared as follows: the imidazolide (**11b**) (0.3 g, 0.8 mmol) and AIBN (0.02 g, 0.1 mmol) in toluene (6 ml) were added to a refluxing solution of Bu_3SnOMe (0.3 g, 1 mmol) in toluene (6 ml) under oxygen-free nitrogen over 20 minutes, and the mixture was refluxed for 1.5 h. Recrystallisation of the oily product gave colourless crystals of the *thiocarbonate* (**26**) (0.1 g, 26%) m.p. 94-96°C (from aq. MeOH); (Found: C, 59.44, H, 5.41. $C_{16}H_{17}ClO_3S$ requires C, 59.16; H, 5.28%); δ_H (60 MHz) 7.30 (4 H, s, ArH), 5.30 (1 H, d, J = 4 Hz, H-2), 4.13 (1 H, s, H-3'), 4.08 (3 H, s, OMe), 2.95 (1 H, brs, H-4) and 1.97 (1 H, brs, H-1); *m/z* M^+ 326/324.

(i) *Bu_3SnD reduction of (E)-endo-2-[imidazol-1-yl(thiocarbonyl)oxy]-3'-(4-chlorophenyl)bicyclo[2.2.1]-heptan-endo-3-spiro-2'-oxirane* (**10b**): D_2-Thioacetal (**25b**) (10%); the ^1H NMR spectrum (250 MHz) was identical to the non-deuteriated (**25b**) except that the ABq at 4.80-5.00 was absent. D_3-*Methoxyoxirane* (**24b**) (21%); m.p. 49.5-51.5°C; the ^1H NMR spectrum was identical to the non-deuteriated (**25b**) except that the methoxy singlet at 3.36 was absent; *m/z* M^+ 269/267 (D_3).

2-Hydroxybenzylbicyclo[2.2.1]hept-2-ene (17a)

(a) *2-Benzylidenebicyclo[2.2.1]heptane*: A solution of diethylbenzylphosphonate (16 g, 68 mmol) in THF (150 ml) was cooled to -78°C under oxygen-free nitrogen. Butyl lithium (4.4 g, 69 mmol) was added, and the mixture was stirred for 30 min and brought to room temperature, left to stand for 30 minutes, cooled to -78°C, and a solution of norcamphor (5.5 g, 50 mmol) in THF was added. The mixture was left to stand for 1 h and stirred overnight at room temperature. The reaction mixture was diluted with water and extracted into Et_2O, washed with water, and brine. The ehter extracts were dried and solvent was evaporated to dryness. The crude product was purified using column chromatography with TLC silica gel as adsorbent and Et_2O:light petroleum as eluant to yield a colourless oil of 2-benzylidenebicyclo[2.2.1]heptane (8 g, 80%). ^1H NMR spectroscopy showed a 3:1 mixture of isomers, δ_H (60 MHz) 7.30 (5 H, s, ArH), 6.30 (1 H, brs, C=CH), 2.87 (1 H, brs, H-4) and 2.30 (1 H, brs, H-1).; υ_{max} (neat) 1655 cm^{-1}.

(b) *3'-Phenylbicyclo[2.2.1]heptan-3-spiro-2'-oxirane:* Epoxidation was carried out using the general procedure (59%); δ_H (60 MHz) 7.20 (5 H, s, ArH), 3.90 (1 H, s, H-3'), 2.34 (1 H, brs, H-1) and 1.95 (1 H, brs, H-4).

(c) *2-Hydroxybenzylbicyclo[2.2.1]hept-2-ene* (**17a**): A solution of the oxirane (0.6 g, 3 mmol) in THF (20 ml) was added to a solution of LDA (made *in situ* by from di-isopropylamine (0.6 g,6 mmol) and n-butyllithium (0.4 g, 6 mmol) at -78°C under oxygen-free nitrogen). The mixture was refluxed for 48 h. The reaction mixture was cooled, poured into water, and extracted with Et_2O. The ether extraxts were washed with 1 M aq. hydrochloric acid, 5% aqueous sodium hydrogen carbonate, and water, dried, and the ether removed *in vacuo*. The residue was purified using column chromatography with TLC silica gel as adsorbent and CH_2Cl_2:light petroleum as eluant. The less polar product was unaltered starting material (33%). The more polar fraction was recrystallised to give *2-hydroxybenzylbicyclo[2.2.1]hept-2-ene* (0.15g, 38%) m.p. 54-55.5°C (aq. EtOH); (Found: C, 83.50; H, 8.11. $C_{14}H_{16}O$ requires C, 83.90; H, 8.05%); υ_{max} 3224 cm^{-1}; δ_H (60 MHz) 7.30 (5 H, s, ArH), 5.90 (1 H, m, H-3), 5.30 (1 H, brs, H-C*H*OH), 2.75 (2 H, m, H-1,4), 2.00 (1 H, s, D_2O exchange, OH); *m/z* (M^+ 200.1201, 20%, $C_{14}H_{16}O$ requires 200.1189).

Alternative synthesis (E)-3'-(4-chlorophenyl)-endo-2-methoxybicyclo[2.2.1]heptan-exo-3-spiro-2'-oxirane (22b)

The allylic alcohol (**4b**) (0.6 g, 2.6 mmol) was added to a suspension of sodium hydride (1 g, 41 mmol) in dry diethyl ether (10 ml) under nitrogen. The mixture was refluxed for 15 min, methyl iodide (4 g, 28 mmol) in dimethylsulphoxide (10 ml) was added over 15 min, and refluxed for a further 30 minutes until the reaction was completed (TLC). Recrystallisation of the oily product from aqueous methanol gave colourless crystals of *(E)*-3-(4-chlorobenzylidene)-*endo*-2-methoxybicyclo[2.2.1]heptane (0.4 g, 63%) m.p. 80-82°C (from aq.

MeOH); δ_H (60 MHz) 7.30 (4 H, s, ArH), 6.30 (1 H, brs, C=CH), 4.10 (1 H, m, H-2), 3.40 (3 H, s, OMe), 3.20 (1 H, brs, H-4) and 2.60 (1 H, brs, H-1); *m/z* M^+ 250/248. The product was epoxidised using the standard procedure to give a mixture of oxiranes which were separated. The methoxy-oxirane (**22b**) was identical (m.p., TLC, IR and 1H NMR spectra) to the material from the Bu_3SnH reduction.

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