Reduction of Substituted Nitro Compounds with Tri-n-butyltin Hydride

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α-Substituted nitro compounds have been reduced with tri-n-butyltin hydride to give replacement of the α-substituent by hydrogen (2-bromo-, 2-chloro- and 2-nitro-2-phenylsulphonylpropane to 2-nitropropane; *p*-nitrobenzyl chloride, bromide, iodide and thiocyanate to *p*-nitrotoluene; 5-nitrofurfuryl nitrate to 2-methyl-5-nitrofuran and 2-hydroxymethyl-5-nitrofuran; 2-(bromomethyl)-1-methyl-5-nitroimidazole to 1,2-dimethylimidazole). 2-Bromo-2-nitrohept-6-ene and 1-bromo-1-nitrohex-5-ene were reduced to 2-nitrohept-6-ene and 1-nitrohex-5-ene, 5-bromo- and 5-phenylsulphonyl-5-nitro-6-phenyl-norborn-6-ene to 5-nitro-6-phenylnorborn-6-ene and 2-iodo-2-nitro-3-(*endo*-norborn-2-en-5-yl)propane to 2-nitro-3-(*endo*-norborn-2-en-5-yl)propane without cyclisation of the intermediate alkenyl α-nitroalkyl radicals. 2-Bromo-2-nitrohex-5-ene and 1-bromo-1-nitropent-4-ene were reduced to the respective nitroalkenes at high [Bu_3SnH] but at lower [Bu_3SnH] cyclisation to 1-methyl-1-nitrocyclopentane and 1-nitrocyclopentane took place. Inhibition studies of the reductions of 2-bromo-2-nitrohex-5-ene and *p*-nitrobenzyl bromide showed a radical chain mechanism. In some of the reductions at low [Bu_3SnH], radical rearrangement of the intermediate α-nitroalkyl radicals gave the respective ketones. Mechanisms involving (*a*) addition/elimination and (*b*) dissociation of intermediate radical anions, are proposed.

Aliphatic nitro compounds and α-substituted aliphatic nitro compounds have been reported[1,2] to be reduced in a number of radical reactions to give replacement of the nitro group, or the α-substituent, by hydrogen. Methanethiolate was initially used[3] as the reductant for tertiary nitro compounds (Scheme 1) and later dihydrobenzylnicotinamide (BNAH) was used for the reduction of α-substituted aliphatic nitro compounds (Scheme 2). Both reductions proceed *via* single electron transfer (SET) and intermediate nitro radical anions. In the BNAH reactions the intermediate radical anions dissociate either by loss of the nitro group, or the α-substituent, depending on the relative nucleofugacity from the respective radical anion (Scheme 2). This competitive loss is the same as that observed in $S_{RN}1$ reactions[5] in which the same dissociative steps [eqns. (2) and (3)] are a central part of the mechanism.

Recently, Tanner *et al.*[6] have reported that α-substituted nitro compounds are reduced by an analogous mechanism using 1,3-dimethyl-2-phenylbenzimidazoline. Sodium hydrogen telluride (NaHTe)[7] also reduces by replacement of the nitro group or the α-substituent by hydrogen suggesting a similar mechanism.

The use of tri-n-butyltin hydride (Bu_3SnH) is the most extensively used procedure for reducing aliphatic nitro compounds. Most reactions have involved the reductive removal of the nitro group[1,2] which can be carried out in the presence of various other functional groups and has many useful synthetic applications. A number of α-substituted nitro compounds have been studied and either the nitro group,[1,2,8–11] or the α-substituent, are replaced by hydrogen [see eqns. (5) and (6)].

$$R_2C(X)NO_2 + Bu_3SnH \longrightarrow R_2CHNO_2 + Bu_3SnX$$
$$X = Cl,^{12}\ SPh,^{13}\ SO_2Ph^6 \quad (5)$$

$$R_2C(X)NO_2 + Bu_3SnH \longrightarrow R_2CHX + Bu_3SnONO$$
$$X = CN, CO_2Me, COPh, Ar, Alkyl, PO_3Et_2 \quad (6)$$

The resulting loss of the nitro group or the α-substituent is the same as observed for BNAH reductions[4] and $S_{RN}1$ substitutions,[5] suggesting that the key step in the radical reduction with Bu_3SnH involves the intermediate radical anion, $[R_2C(X)NO_2]^{-\bullet}$ [eqns. (2) and (3)]. However, two different mechanisms have been proposed to explain the reduction. Both of these mechanisms are backed by experimental evidence which clearly indicates a radical chain mechanism.[8–12] The first proposal[9,12] (Scheme 3) involves the dissociation of an intermediate nitro radical anion as proposed for BNAH

$$R_3CNO_2 + CH_3S^- \xrightarrow{SET} (R_3CNO_2)^{-\bullet} + CH_3S^\bullet \quad \text{initiation}$$

propagation steps:

$$(R_3CNO_2)^{-\bullet} \longrightarrow R_3C^\bullet + NO_2^-$$
$$R_3C^\bullet + CH_3S^- \longrightarrow R_3CH + (CH_2{=}S)^{-\bullet}$$
$$R_3CNO_2 + (CH_2{-}S)^{-\bullet} \longrightarrow (R_3CNO_2)^{-\bullet} + CH_2{=}S$$

Scheme 1 Reduction of aliphatic nitro compounds with methanethiolate

$$R_2C(X)NO_2 + (BNA)^\bullet \xrightarrow{SET} [R_2C(X)NO]^{-\bullet} + (BNA)^+ \quad (1)$$
$$[R_2C(X)NO_2]^{-\bullet} \longrightarrow R_2\dot{C}{-}NO_2 + X^- \ [X = Br, Cl, SO_2Ph] \quad (2)$$
$$\longrightarrow R_2\dot{C}{-}X + NO_2^- \ [X = COR, CO_2Et, CN] \quad (3)$$
$$R_2\dot{C}{-}NO_2\ (R_2\dot{C}{-}X) + BNAH \longrightarrow R_2CHNO_2\ (R_2CHX) + (BNA)^\bullet \quad (4)$$

Scheme 2 Reduction of α-substituted nitro compounds with dihydrobenzylnicotinamide (BNAH)

$$R_2C(X)NO_2 + Bu_3Sn^{\bullet} \xrightarrow{SET} [R_2C(X)NO_2]^{-\bullet} + Bu_3Sn^+$$

$$[R_2C(X)NO_2]^{-\bullet} \longrightarrow R_2\dot{C} - NO_2 + Br^-$$

$$\longrightarrow R_2\dot{C} - X + NO_2^-$$

$$R_2\dot{C}\text{–}NO_2\ (R_2\dot{C}\text{–}X) + Bu_3SnH \longrightarrow R_2CHNO_2\ (R_2CHX) + Bu_3Sn^{\bullet}$$

Scheme 3 Bu_3SnH reduction mechanism *via* an intermediate radical anion

$$R_2C(X)NO_2 + Bu_3Sn^{\bullet} \longrightarrow R_2C(X)\text{–}N(O^{\bullet})\text{–}O\text{–}SnBu_3$$

$$R_2C(X)\text{–}N(O^{\bullet})\text{–}O\text{–}SnBu_3 \longrightarrow R_2\dot{C}\text{–}X + Bu_3Sn\text{–}ONO$$

$$R_2\dot{C}\text{–}X + Bu_3SnH \longrightarrow R_2CHX + Bu_3Sn^{\bullet}$$

Scheme 4 Bu_3SnH reduction mechanism *via* an intermediate nitroxide

Table 1 Reduction of substituted nitro compounds with Bu_3SnH

Substrate	Reaction conditions[a]	Bu_3SnH equiv.	Products	Yield (%)	Unchanged starting material (%)
$Me_2C(Br)NO_2$	PhH, 8 h	1.2	Me_2CHNO_2	66	0
$Me_2C(Cl)NO_2$	PhH, 19 h	1.2	Me_2CHNO_2	47	3
$Me_2C(SO_2Ph)NO_2$	MeCN, 70 h	3.0	Me_2CHNO_2	32	15
p-NO_2–$C_6H_4CH_2Cl$	3 h	2.17	p-Nitrotoluene	24	77
p-NO_2–$C_6H_4CH_2SCN$	3 h	2.17	p-Nitrotoluene	32	55
p-NO_2–$C_6H_4CH_2I$	3.5 h	2.17	p-Nitrotoluene	71	0
p-NO_2–$C_6H_4CH_2Br$	1 h	2.17	p-Nitrotoluene	30	51
	3 h	2.17	p-Nitrotoluene	60	10
	4 h	2.17	p-Nitrotoluene	75	0
	Reflux 1 h	2.17	p-Nitrotoluene	47	0
	Reflux 2 h	2.17	p-Nitrotoluene	60	0
	90 min	2.09	p-Nitrotoluene	45	52
	90 min $Bu^t_2NO^{\bullet}$ (60 mol %)	2.09	p-Nitrotoluene	0	33
	90 min, dark	2.09	p-Nitrotoluene	0	88
	90 min, dark reflux	2.09	p-Nitrotoluene	100	0
	90 min p-dinitrobenzene (25 mol %)	2.09	p-Nitrotoluene	0	100
	90 min, no AIBN	2.09	p-Nitrotoluene	91	15
	90 min, O_2	2.09	p-NO_2–$C_6H_4CH_2OH$	31	0
p-NO_2–$C_6H_4C(Me)_2NO_2$	47 h Reflux	2.09	p-Nitrocumene	0	80

[a] Reactions were carried out in toluene under an atmosphere of nitrogen and the addition of AIBN (*ca.* 0.2 equiv.) unless otherwise stated.

reductions and $S_{RN}1$ substitutions. The second proposal[2,8,10] involves an addition/elimination mechanism leading to abstraction of the nitro group by the $Bu_3Sn^{\bullet}$ radical (Scheme 4). This mechanism can only be used to explain reductive replacement of nitrite. Studies involving α-substituted nitro compounds in which the α-substituent may be reductively replaced are limited, and with one exception,[12] contain no mechanistic details.

As part of our studies of alkenyl α-nitro alkyl radicals, the reduction with Bu_3SnH of a number of α-substituted nitro compounds was investigated. In order to investigate further the mechanism and to develop the synthetic application we also studied a wider range of representative α-substituted nitro compounds. In this paper, we report the results of both of these studies and attempt to draw mechanistic conclusions.

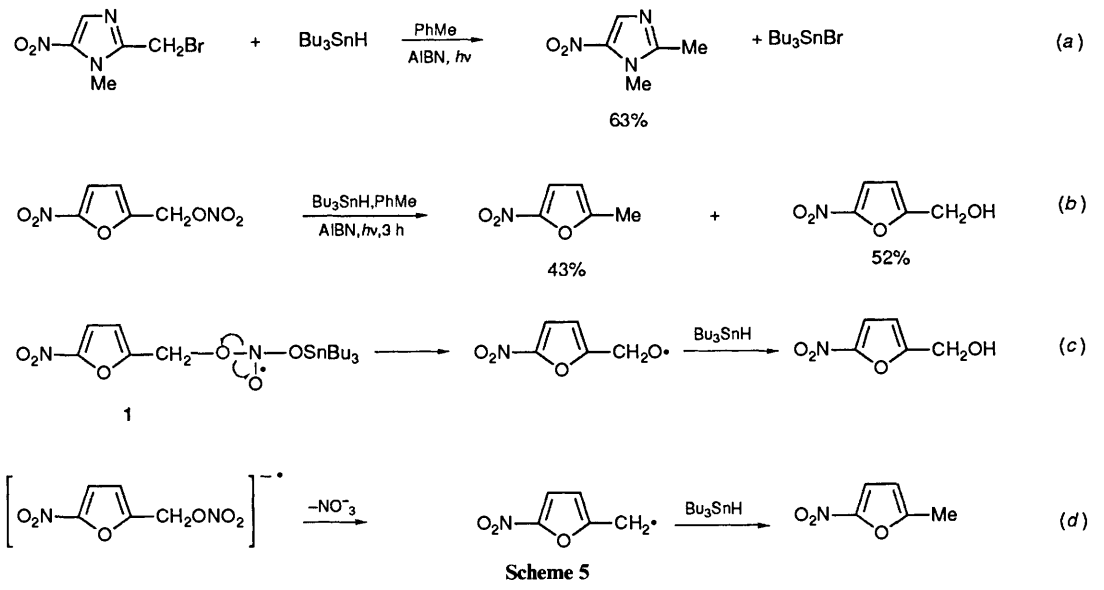
Results and Discussion

The results of the Bu_3SnH reduction of a representative group of α-substituted nitro compounds are presented in Table 1.

2-Chloro- and 2-bromo-2-nitropropane were readily reduced at room temperature with Bu_3SnH to yield selectively 2-nitropropane. No 2-chloro or 2-bromopropane was detected indicating selective loss of the α-substituent. 1-Methyl-1-nitroethyl phenyl sulphone [$Me_2C(SO_2Ph)NO_2$] has been reported to be inert to Bu_3SnH[1,2,8,11] but a footnote in a paper by Tanner[6] indicates reductive loss of the benzenesulphonyl group to yield 2-nitropropane. Our results also indicate a slow reaction which is not unexpected because $S_{RN}1$ reactions[5] of α-nitro sulphones are sluggish and the radical anion is particularly stable as compared with the radical anions of $Me_2C(Br)NO_2$ and $Me_2C(Cl)NO_2$.[14] This result suggests that the Bu_3SnH reduction of the sulphone proceeds by a similar mechanism (*i.e.* Scheme 3) to the BNAH reduction and indicates that an addition/elimination mechanism (Scheme 4) is not sufficient to explain all the results.

We considered that an examination of other α-substituted nitro compounds, in which the substituent and nitro group are conjugatively separated and known to undergo $S_{RN}1$ reactions *via* dissociation of intermediate radical anions, would be helpful. p-Nitrobenzyl chloride, bromide, iodide and thiocyanate were all readily reduced with Bu_3SnH to yield p-nitrotoluene as the sole product.

The reduction of p-nitrobenzyl bromide was inhibited using radical traps (di-t-butyl nitroxide and oxygen). In the oxygen inhibition reaction, p-nitrobenzyl alcohol was formed indicating



Scheme 5

Table 2 Bu_3SnH reductions of alkenyl α-bromonitroalkanes

Substrate	[Bu_3SnH] /mol dm^{-3}	Yield (%) Unaltered substrate	Nitroalkene	Ketone	Cyclised product
2-Bromo-2-nitrohept-6-ene[a,b]	0.36	—	68 (**3**)	25 (**4**)	0
	0.01	22	39 (**3**)	2 (**4**)	0
2-Bromo-2-nitrohex-5-ene[a,c]	0.36	—	60 (**8**)	0 (**9**)	0(**11**)[d]
	0.15	2	64 (**8**)	0 (**9**)	0(**11**)[d]
	0.072	2	32 (**8**)	<1 (**9**)	15(**11**)[d]
	0.072[e]	33	5 (**8**)	<1 (**9**)	<1(**11**)[d]
	0.072[f]	42	3 (**8**)	<1 (**9**)	<2(**11**)[d]
	0.072[g]	45	3 (**8**)	<1 (**9**)	<2(**11**)[d]
	0.01	<1	16 (**8**)	<1 (**9**)	13(**11**)[d]
	0.005	12	1 (**8**)	16[h] (**9**)	6(**11**)[d]
1-Bromo-1-nitrohex-5-ene[a,b,i]	0.085	2	59 (1-nitrohex-5-ene)	—	10[j]
1-Bromo-1-nitropent-4-ene[a,b]	0.01	2	44 (1-nitropent-4-ene)	—	0

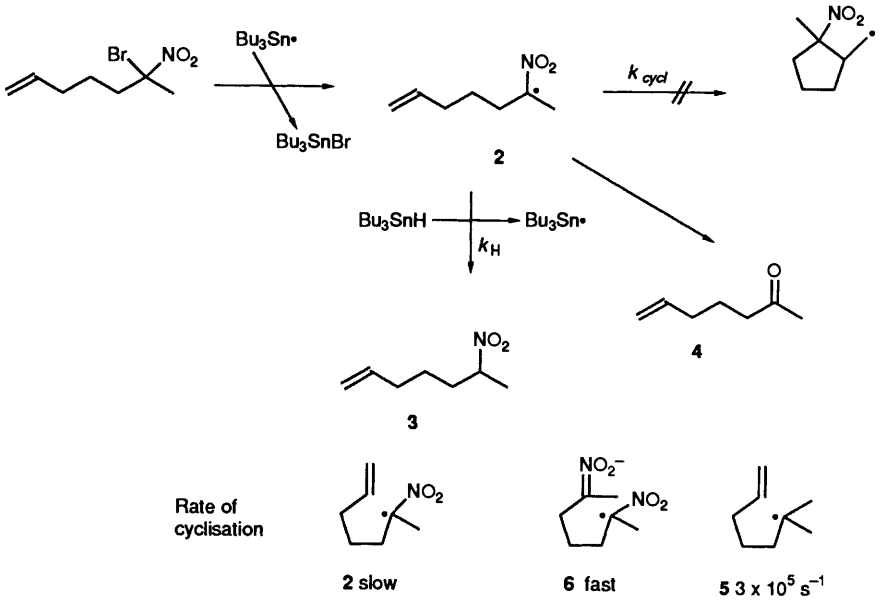
[a] Bu_3SnH (1.1 equiv.), AIBN (10 mol %), N_2, *hv*, 40 °C. [b] Toluene used as the solvent. [c] Benzene used as the solvent. [d] 1-Methyl-1-nitrocyclopentane (**11**). [e] Dark, no AIBN. [f] *p*-Dinitrobenzene (25 mol %). [g] O_2 in place of N_2. [h] 11% of 2-hydroxyhex-5-ene was also present. [i] *ca.* 20% of an unidentified product. [j] No nitrocyclohexane, 1-methyl-2-nitrocyclopentane (11%, not fully characterised).

trapping of the *p*-nitrobenzyl radical by oxygen.[3,19] The reduction was also shown to be catalysed by light or thermally initiated. Azobis(isobutyronitrile) (AIBN) catalysed the reaction but was not essential. Strong electron acceptors (*p*-dinitrobenzene and oxygen) also inhibited the reaction suggesting intermediate radical anions. However, as pointed out in the literature,[8] *p*-dinitrobenzene is also a good trap for $Bu_3Sn^{\bullet}$ radicals and therefore use of this inhibitor does not necessarily indicate radical anions in the chain mechanism.

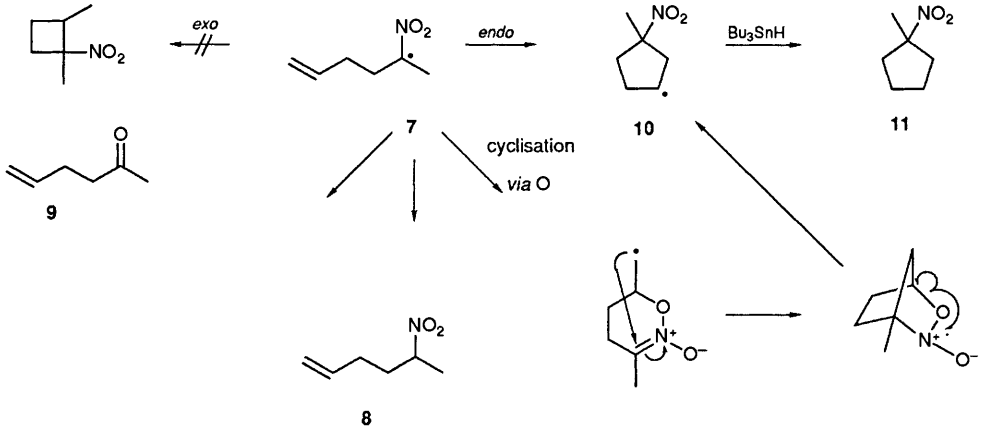
The analogous 5-nitroimidazole and 5-nitrofuran compounds gave similar results [Scheme 5(*a*), (*b*)]. Similarly to the nitrobenzyl compounds, the nitroimidazole- and the nitrofuran-derivatives have been shown to undergo $S_{RN}1$ reactions[15,16] and their radical anions have been observed by EPR spectroscopy[17,18] and exhibit the same dissociative behaviour. The 52% yield of 2-hydroxymethyl-5-nitrofuran indicates that the addition/elimination mechanism *via* an intermediate nitroxide (**1**) is partially or fully in operation [Scheme 5(*c*)]. However the formation of 2-methyl-5-nitrofuran (40%) is better explained by the dissociation of the intermediate radical anion as observed in $S_{RN}1$ reactions [Scheme 5(*d*)].

2-Nitro-2-(4-nitrophenyl)propane was completely unreactive even after prolonged heating and no sign of *p*-nitrocumene was observed. This result supports the reported inertness to Bu_3SnH.[2,11] In contrast, the analogous *p*-cyano- and *p*-methoxy-nitrocumenes were readily reduced.[2,8,11] 2-Nitro-2-(4-nitrophenyl)propane does slowly undergo $S_{RN}1$ reactions[3,5,19] and the radical anion does dissociate to *p*-nitrocumyl radicals.[20] The suggestion[11] that $Bu_3Sn^{\bullet}$ radicals selectively attack the aromatic nitro group to yield a nitroxide in which the C–N bond is unlikely to break, appears correct. The results suggest that the radical anion is not present at any time otherwise reduction to *p*-nitrocumene would be predicted. It is difficult to explain why this should happen for the reduction of 2-nitro-2-(4-nitrophenyl)propane and not for the *p*-nitrobenzyl and related heterocyclic analogues.

Bu_3SnH *Reductions of Alkenyl α-Substituted Nitroalkanes.*— Bu_3SnH reductions of alkenyl α-nitroalkanes were carried out with the aim of studying the cyclisation of the intermediate alkenyl α-nitroalkyl radicals. The results are presented in Table 2. We initially chose the simplest systems expected to exhibit



Scheme 6 Bu_3SnH reductions of 2-bromo-2-nitrohept-6-ene



Scheme 7 Bu_3SnH reduction of 2-bromo-2-nitrohex-5-ene

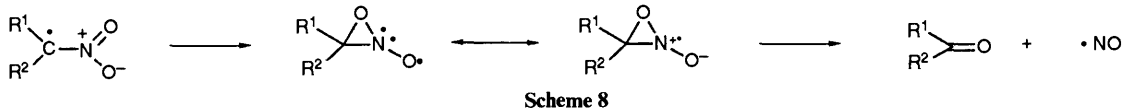
exo-cyclisation (Scheme 6). 2-Bromo-2-nitrohept-6-ene yielded 2-nitrohept-6-ene and hept-6-en-2-one. Lower concentrations of Bu_3SnH did not favour cyclisation as expected, but gave uncharacterised volatile compounds, which may indicate further reduction of the products to yield heptene *etc.* 1-Bromo-1-nitrohex-5-ene also yielded the non-cyclised, 1-nitrohex-5-ene, but with an uncharacterised product which had the same GLC t_R as 1-methyl-2-nitrocyclopentane.

The lack of cyclisation was surprising, but during our studies, Russell and Dedolf[12] reported similar results (the α-nitroalkyl radicals, $CH_2{=}CH(CH_2)_3\dot{C}(Me)NO_2$, generated in $S_{RN}1$ reactions did not cyclise, and 1-cyclopropyl-1-nitro-1-ethyl, generated by Bu_3SnH reduction of 1-cyclopropyl-1-chloro-1-nitroethane, failed to undergo ring-opening). Obviously the rate of abstraction of hydrogen from Bu_3SnH (k_H) by the intermediate radical **2** is faster than cyclisation (k_{cycl}) or conversion into hept-6-en-2-one. All of these rates are unknown but comparison with alkyl analogues is instructive. The rate of cyclisation[21] of 2-methylhept-6-en-2-yl radicals **5** at 30 °C is 3.5×10^5 s^{-1} and the rate of abstraction of hydrogen[22] from Bu_3SnH by $Me_2\dot{C}H$ radicals is 1.5×10^6 dm^{-3} mol^{-1} s^{-1}, *i.e.* abstraction is only faster at high concentrations of Bu_3SnH. We suggest that polarity effects and radical philicity must be taken into account,[23] *i.e.* the highly electrophilic α-nitroalkyl radical **2** will react much faster than the nucleophilic radical **5** with Bu_3SnH, a site of high electron density ($Bu_3Sn^•$ is a strongly nucleophilic radical[23]). A similar effect is predicted for the cyclisation of **2** because the alkene is also nucleophilic, but because it is only weakly nucleophilic this effect is likely to be less marked. This latter suggestion is supported by the rapid cyclisation of the analogous α-nitroalkyl radical with the strongly nucleophilic nitronate **6**.[24]

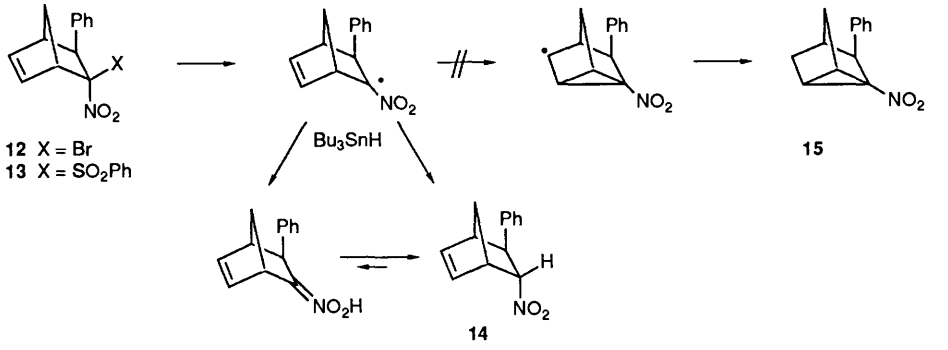
Equilibrium between cyclised and open chain forms, as observed[25] for analogous stabilised radicals, *e.g.* $CH_2{=}CH(CH_2)_3\dot{C}(CN)CO_2Me$, could possibly explain the lack of cyclisation. However, the α-nitroalkyl radical is not particularly stabilised by the nitro group which has similar radical stabilising to that of a methyl group.[14,26] Therefore, we propose that the strongly electrophilic α-nitroalkyl radicals only cyclise faster than abstraction from Bu_3SnH when a strongly nucleophilic unsaturated group (*e.g.* nitronate) is present.

2-Bromo-2-nitrohex-5-ene was also reduced with Bu_3SnH at various concentrations (Table 2, Scheme 7). At the higher [Bu_3SnH] (0.36 mol dm^{-3}), only the nitroalkene **8** was formed, and at very low concentration (0.005 mol dm^{-3}), largely pent-4-en-2-one **9**. At 0.072 mol dm^{-3} concentration, a new product, with t_R (on several different GLC columns) identical with authentic 1-methyl-1-nitrocyclopentane, was observed. Unfortunately, even exhaustive attempts at separation of pure material for positive characterisation failed.

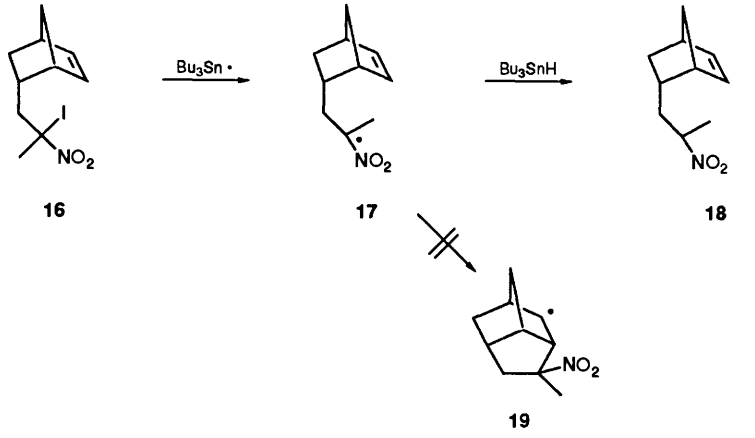
Inhibition studies showed that all three products were formed by a radical chain process. *exo* Four-membered ring cyclisation is not normally favoured because the reverse reaction is faster



Scheme 8



Scheme 9 **12**: 8 h, 40 °C, 100%; **13**: 18 h, 40%, reflux



[Bu_3SnH] = 0.03 mol dm^{-3} PhH, 40°C, 36 h, N_2, *hν*

Scheme 10 Bu_3SnH reduction of 2-iodo-2-nitro-3-(*endo*-norborn-2-en-5-yl)propane

due to ring strain, and *endo* five-membered ring cyclisation is rare except for stabilised radicals. This apparent *endo* five-membered ring cyclisation to the intermediate radical **10** is possibly explained by *exo* six-membered ring cyclisation *via* the *O*-centre of the nitro radical to give an *exo* radical which rearranges to **10** (Scheme 7). A thermodynamic equilibrium[25] between cyclised and non-cyclised radicals could also explain the *endo*-product. 1-Bromo-1-nitropent-4-ene yielded only the non-cyclised product, 1-nitropent-4-ene.

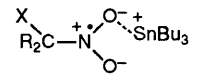
In the reduction of 2-bromo-2-nitro-hept-6-ene and -hex-5-ene, the ketones **4** and **9** were formed at low [Bu_3SnH]. Rearrangement of α-nitroalkyl radicals to ketones has been reported [see eqn. (11)].[24,27] This unimolecular rearrangement of the intermediate radicals **2** and **7** to hept-6-en-2-one and hex-5-en-2-one, respectively, would be favoured over bimolecular reaction with Bu_3SnH at low [Bu_3SnH]. Rearrangement of **2** is faster than cyclisation but rearrangement of **7** only overrides cyclisation at very low [Bu_3SnH]. This requires slow ring opening of the cyclised radical **10** to **7** when the bimolecular reduction of **10** with Bu_3SnH becomes unfavourable. Inhibition of ketone formation indicates a radical route of formation (Scheme 8).

Because of the failure of facile cyclisation of alkenyl α-nitroalkyl radicals, we used alkenylalkyl radicals in which the alkene is known to be orientated towards cyclisation. The bicyclo[2.2.1]oct-5-en-2-yl system was investigated first (Scheme 9). The bromo(nitro)norbornene **12**, gave a quantitative yield of the nitronorbornene **14** at room temperature (Scheme 9). The sulphonyl derivative **13** reacted slowly to give a moderate yield of the nitronorbornene **14** confirming the results with $Me_2C(SO_2Ph)NO_2$ that α-nitro sulphones are reduced with replacement of the sulphonyl group and not the nitro group. None of the cyclised material **15** was detected, again indicating that reduction of the intermediate α-nitroalkyl radical by Bu_3SnH is faster than cyclisation. The α-nitroalkyl radical is ambient and therefore hydrogen can be abstracted from Bu_3SnH by either the oxygen or carbon atoms. The nitronate if formed would rapidly tautomerise to the *endo*-nitronorbornene **14**.

The fastest rate of cyclisation of an alkenylalkyl radical has been reported for the *exo* five-membered ring cyclisation of 2-(*endo*-norborn-2-en-5-yl)ethyl radicals (1×10^7 s^{-1}).[28] Bu_3SnH reduction of 2-iodo-2-nitro-3-(*endo*-norborn-2-en-5-yl)propane **16** gave a *ca.* quantitative yield (analysis by ^1H NMR spectroscopy) of the nitroalkene **18** with no signs of cyclisation of the intermediate radical **17** to **19**. We have shown[29] that cyclisation of **17** to **19** can take place under particularly favoured conditions (photolysis of the α-iodo nitro compound **16** and oxidative addition to the nitronate anion of **18**) which further indicates that the bimolecular reduction of the electrophilic alkenyl α-nitroalkyl radicals by the nucleophilic Bu_3SnH is faster than cyclisation.

All of these alkenyl α-substituted nitro-compounds lost the α-substituent (I, Br, SO_2Ph) rather than the nitro group.

Mechanism of Bu_3SnH *Reduction of α-Substituted Nitro Compounds.*—Both mechanisms (Schemes 3 and 4) indicate that the last step is hydrogen abstraction from Bu_3SnH by the



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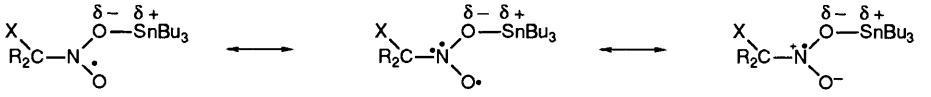

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intermediate radical. The difficulty is determining the nature of the initial reactive intermediate which breaks down to give the intermediate $R_2\dot{C}$–NO_2 or $R_2\dot{C}$–X radicals. The SET mechanism[9,12] is supported by the ease of oxidation of $Bu_3Sn^{\bullet}$ radicals to yield Bu_3Sn^+ cations (Scheme 3). An equilibrium between the unassociated radical anion and the nitroxide intermediates is possible, and loss of NO_2 *via* an addition/elimination mechanism (Scheme 4) only takes place when loss of the α-substituent (X) from the radical anion is not favoured [eqn. (7)]. Loss of the α-substituent (except for $PhSO_2$) is fast (several hours at room temperature) in these reductive reactions whereas loss of NO_2 is slow and only takes place after hours of reflux. Loss of NO_2 is faster in the Bu_3SnH reductions than in 'pure' radical anion reactions, which supports the addition/elimination mechanism for compounds in which NO_2 is lost instead of the α-substituent.

$$R_2\dot{C}\text{–}NO_2 + X^- \longleftarrow [R_2C(X)NO_2]^{-\bullet} + Bu_3Sn^+ \quad (7)$$
$$\rightleftharpoons [R_2C(X)NO_2SnBu_3]^{\bullet} \longrightarrow R_2\dot{C}\text{–}X + Bu_3SnONO$$

The dichotomy between the addition/elimination mechanism (intermediate nitroxide, Scheme 4) and the SET mechanism (intermediate radical anion and Bu_3Sn^+ cation, Scheme 3) is possibly false. Giese *et al.*[10,30] initially proposed a close ion pair (**20**) to explain the small Sn hyperfine coupling observed in the EPR spectrum of the intermediate, and later, Giese[30] and Ono[2,8] proposed that a nitroxide (**21**) was a better explanation. The difference between the nitroxide, close ion pair, and unassociated radical anion and Bu_3Sn^+, is the percentage of ionic/character in the intermediate species. Similar nitroxide intermediates have been proposed for the reaction of trialkyl-lead[31,32] and -silicon[33] radicals with nitro compounds.

If the canonical forms of the proposed nitroxide intermediate are considered, one form, (**22**) is little different from the 'close ion pair' **20** and both can be considered the Bu_3Sn-ester derivative of the nitro radical anion. This proposal is born out by the EPR spectral data of the nitroxides (a_N = 26.1–28.8 G)[8,10,30] and the radical anions (a_{iso} = 23.7–29.3 G and similar data for solution-phase spectra),[14] *i.e.* whatever the nature of the actual intermediate, it has dominant radical-anion character, but with association of the Sn moiety. EPR spectroscopy has shown[14] that the unpaired electron in the radical anions of α-substituted nitro compounds is shared between the nitro π* and C–X σ* molecular orbitals and that the dissociation proceeds by loss of nitrite (X = COR, CO_2R, CN, R) or the α-substituent (X = Hal, SCN, SR, SO_2Ar) depending on the relative nucleofugacity. The same nucleofugacity has been observed in the Bu_3SnH reactions, *i.e.* the substituent (NO_2 or X) when lost is associated with the Bu_3Sn moiety (Bu_3Sn–X or Bu_3Sn–ONO).

These concepts can also be applied to the *p*-nitrobenzyl and related 5-nitrofurfuryl and 5-nitroimidazole analogues as EPR spectroscopy[17,18,20] has shown the unpaired electron in the radical anions is shared between the nitro π* and benzylic C–X σ* molecular orbitals, *i.e.* attachment of $Bu_3Sn^{\bullet}$ radicals to the aromatic nitro group will allow dissociation *via* loss of the 'benzylic' substituent. The behaviour of 2-nitro-2-(4-nitrophenyl)propane remains unexplained.

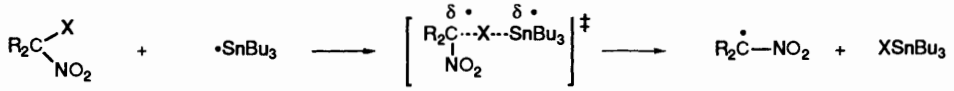
The stability of the resulting radicals is unlikely to be a major factor as has been suggested,[10] *e.g.* α-nitro sulphides [$R_2C(SAr)NO_2$] lose thiolate to give $R_2\dot{C}$–NO_2 radicals which are less stable than the alternative $R_2\dot{C}$–SAr radicals which would result from nitrite abstraction. The stability of the resulting radicals will lower the transition-state energy in the addition/elimination type mechanism, *e.g.* tertiary nitro ≫ secondary nitro and primary nitro does not react.

A third explanation is that an addition/elimination mechanism takes place for loss of X or NO_2, whichever is most favourable, as shown in Scheme 11 and Scheme 4. Attack by the nucleophilic $Bu_3Sn^{\bullet}$ radical[23] on the α-substituent (which has low electron density because of the strong $-I$ inductive effect of the nitro-group) by a fast S_H2 mechanism [eqn. (13)] is favoured for X = Hal, SCN, SR, SO_2Ar. A similar mechanism has been proposed for the Bu_3SnH reduction of α-keto sulphones to ketones.[33] This explanation would also explain why chlorine is abstracted faster from $Me_2C(Cl)NO_2$ than from benzyl chloride by Bu_3SnH.[12] A slower abstraction of NO_2 (Scheme 4) is only favoured when the α-substituent cannot be abstracted (X = COR, CO_2R, CN, R). Similarly, the α-substituents of $R_2C(X)NO_2$[5,34] and the *p*-nitrobenzyl and related compounds[5,35] are also susceptible to polar nucleophilic abstraction by strong nucleophiles such as thiolates, even when SET is strongly favoured.

Experimental

General.—^{1}H NMR spectra were measured using a Varian EM360 spectrometer at 60 MHz with $CDCl_3$ as the solvent and tetramethylsilane (TMS) as the internal reference. *p*-Dimethoxybenzene was used as an internal standard to measure yields of products in mixtures by ^{1}H NMR spectroscopy. HPLC analyses (reversed phase) were carried out on a Pye-Unicam 4020 UV detector set at 230 nm. A Hypersil ODS column with acetonitrile–water (50:50 v/v) as the eluant with a 20 mm^3 injection loop were used. Methanol–water (70:30 v/v) was used as the eluant for the analysis of *p*-nitrobenzyl chloride reactions. GLC analyses using FID were carried out on a Carlo-Erba GC6000 Vega apparatus with a SGE BP1 12 m capillary column and a Pye 104 apparatus with a 5 ft standard glass column of 10% Carbowax. 2-Methyl-2-nitropropane and nitrocyclohexane were used as internal standards with calibrations for each component. Tungsten 'white light' fluorescent lamps (2 × 150 W) (mercury blended) were used for irradiation studies.

Materials.—2-Bromo- and 2-chloro-2-nitropropane,[36] 1-methyl-1-nitroethyl phenyl sulphone,[37] 5-nitrofurfuryl nitrate,[38] 2-nitro-2-(4-nitrophenyl)propane,[19] 2-(bromomethyl)-1-methyl-5-nitroimidazole,[39] 2-methyl-5-nitrofuran[16] and 1,2-dimethylimidazole[15] were prepared by literature procedures. 2-Bromo-2-nitro-hept-6-ene and -hex-5-ene were prepared[29] from hept-6-en-2-one and hex-5-en-2-one respectively *via* the corresponding oximes and α-bromo-nitroso compounds. 1-



Scheme 11

Bromo-1-nitro-hex-5-ene and -pent-4-ene were prepared by NBS bromination[29] of the anions of the respective ω-nitroalkenes.[40] 2-Nitro-hex-5-ene and -hept-6-ene were prepared by sodium borohydride reduction of the respective bromo nitro compounds.[29] 1-Methyl-1-nitrocyclopentane was prepared by oxidation of 1-amino-1-methylcyclopentane[41] which in turn was prepared by a modified Ritter reaction from 1-hydroxy-1-methylcyclopentane.[42] 5-Nitro-6-phenylnorborn-2-ene (**14**) was prepared by a Diels–Alder reaction between cyclopentadiene and (*E*)-β-nitrostyrene.[43] The bromo derivative **12** was prepared by bromination of the nitronate anion,[29] and the phenylsulphonyl derivative **13** was prepared by oxidative addition of sodium benzenesulphinate to the nitronate anion.[29] 2-Nitro-3-(*endo*-norborn-2-en-5-yl)propane (**18**) was prepared[29] from 2-norbornene-5-carbaldehyde and iodination of the nitronate anion[29] gave the α-iodo nitro derivative **16**.

Reduction of 2-*Substituted* 2-*Nitropropanes with* Bu_3SnH.—The 2-substituted-2-nitropropane (2.5 mmol), Bu_3SnH (3.0 mmol) and AIBN (0.4 mmole) were dissolved in dry distilled benzene (15 cm^3) in a Carius tube. The solution was deoxygenated with nitrogen, frozen and the tube sealed. The sealed solution was irradiated for the chosen time. On completion of the reaction the tube was opened, the solution made up to 25 cm^3 in MeOH and analysed by HPLC. The results are presented in Table 1.

Reduction of p-*Nitrobenzyl Bromide with* Bu_3SnH.—*General procedure for reductions.* A solution of *p*-nitrobenzyl bromide (0.51 g, 2.4 mmol) and Bu_3SnH (1.50 g, 5.2 mmol) in toluene (15 cm^3) was stirred under a stream of nitrogen for 40 min. AIBN (0.10 g, 0.6 mmol) in toluene (5 cm^3) was added and the solution irradiated for 3 h. The solvent was removed *in vacuo* to give an orange oil, which was directly analysed by means of ^1H NMR spectroscopy and/or made up to 25 cm^3 with MeOH and analysed by HPLC. The reaction was repeated using different times.

p-Nitrobenzyl chloride, iodide and thiocyanate, and 5-nitrofurfuryl nitrate were reacted under the same conditions. 2-Nitro-2-(4-nitrophenyl)-propane was reacted, using the general procedure, at reflux for 48 h.

Inhibition studies were carried out with *p*-nitrobenzyl bromide for a standard time of 90 min using the same conditions as above except as detailed below: (*a*) di-t-butyl nitroxide (60 mol %) was added with the AIBN; (*b*) the reaction was carried out with the exclusion of light which was effected by wrapping the reaction flask in aluminium foil; (*c*) *p*-dinitrobenzene (25 mol %) was added with the AIBN; (*d*) oxygen was used in place of nitrogen; (*e*) no AIBN was added; (*f*) the reaction was carried out with the exclusion of light and under reflux. The results of all these reactions are reported in Table 1.

Reduction of 2-*Bromomethyl*-1-*methyl*-5-*nitroimidazole with* Bu_3SnH.—2-Bromomethyl-1-methyl-5-nitroimidazole (1.406 g, 6.39 mmol), Bu_3SnH (3.0 g, 13 mmol) and AIBN (0.10 g, 0.6 mmol) in toluene (60 cm^3) were allowed to react for 5 h using the general procedure. The reaction solution was evaporated to dryness and the resulting residue dissolved in dichloromethane and extracted with dil. hydrochloric acid (2 mol dm^{-3}). The acid solution was washed with diethyl ether, basified with sodium carbonate and extracted with dichloromethane. The solution was evaporated to dryness to yield pure 1,2-dimethyl-5-nitroimidazole (0.57 g, 63%). The product was recrystallised (H_2O/MeOH) to give colourless crystals of 1,2-dimethyl-5-nitroimidazole, m.p. 134–135 °C (lit.,[39] 135–136 °C). The IR and ^1H NMR spectra were identical with that of authentic material.

Bu_3SnH *Reduction of Alkenyl* α-*Substituted Nitroalkanes.*—The general procedure was used for the reductions of 2-bromo-2-nitro-hept-6-ene and -hex-5-ene, 1-bromo-1-nitro-hex-5-ene and -pent-4-ene, 5-bromo- and 5-phenylsulphonyl-5-nitro-6-phenylnorborn-2-ene (**12**) and (**13**), and 2-iodo-2-nitro-3-(*endo*-norborn-2-en-5-yl)propane (**16**) with Bu_3SnH (1.1 equiv.) and AIBN (10 mol %) in toluene or benzene at 40 °C with light catalysis. The crude products were analysed by ^1H NMR spectroscopy or GLC. The time of the reaction and concentration of Bu_3SnH are reported in the discussion. The inhibition reactions with 2-bromo-2-nitrohept-6-ene were carried out as outlined in the general procedure for Bu_3SnH reactions (see Table 2 for data).

In the reductions of the α-bromo- and α-phenylsulphonyl-norbornenes (**12** and **13**) ([Bu_3SnH] = 0.3 mol dm^{-3}, toluene), the crude product mixtures, analysed by ^1H NMR spectroscopy, showed 5-nitro-6-phenylnorborn-2-ene as the sole product (100 and 40%, respectively). The crude reaction mixture was reacted with sodium methoxide to form the anion of the nitro compound **14**. The tin residues and starting material were extracted with diethyl ether from an aqueous solution of the nitronate. Neutralisation of the nitronate with hydroxylamine hydrochloride and extraction with diethyl ether gave the pure 5-nitro-6-phenylnorborn-2-ene after recrystallisation (20 and 19%, respectively).

Extensive attempts to isolate and characterise fully 1-methyl-1-nitrocyclopentane from the reduction of 2-bromo-2-nitro-hept-6-ene, 1-methyl-2-nitrocyclopentane from 1-bromo-1-nitrohex-5-ene, and 2-nitro-3-(*endo*-norborn-2-en-5-yl)propane (**18**) from 2-iodo-2-nitro-3-(*endo*-norborn-2-en-5-yl)propane (**16**), failed owing to the similarity with tin residues.

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