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Ring closure of 2-thia- and 2-sulfonyl-5-hexenyl radicals

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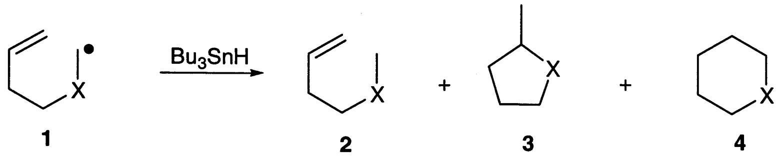
Abstract

Reductive cyclisation of the 2-sulfonyl-5-hexenyl radical with tributyltin hydride in benzene at 80°C affords a 73:23 mixture of the sulfones derived from 5-*exo*- and 6-*endo*- ring closure with a small quantity (4%) of reduced material; under identical conditions, the 2-thia-5-hexenyl radical gives a 70:13:17 mixture of the corresponding sulfides. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: α-thia radicals; α-sulfonyl radicals; radical cyclisation; heterocyclic synthesis.

Ring closure of 5-hexenyl radicals is a valuable synthetic process which generally leads to the construction of cyclopentane derivatives. The overwhelming preference for the 5-*exo* product is a consequence of a dominant stereoelectronic effect and, when a hetero atom is incorporated in the chain, cyclisation represents a potentially useful procedure for the synthesis of heterocyclic compounds. In the case of radicals where an atom with lone pair electrons such as O, N, or S occupies a position α to the radical centre, significant differences have emerged. Thus, the oxygen-based 5-hexenyl species **1** (X = O) has been reported[1] to cyclise with high regioselectivity to give the tetrahydrofuranyl isomer **3** (X = O) in excellent yield.



In contrast, the corresponding α-amino radical **1** (X = NR) resists ring closure and gives the product of reduction **2** (X = NR) exclusively.[2] We have demonstrated[3] that quaternisation of the amine removes the stabilising influence of the nitrogen lone pair; for example, the α-ammonium species **1** ($X = Me_2N^+$) undergoes ring closure with high regioselectivity to furnish the pyrrolidinium salt **3** ($X = Me_2N^+$). Neither the reduction product **2** ($X = Me_2N^+$) nor the isomeric 6-*endo* product **4** ($X = Me_2N^+$) were detected.

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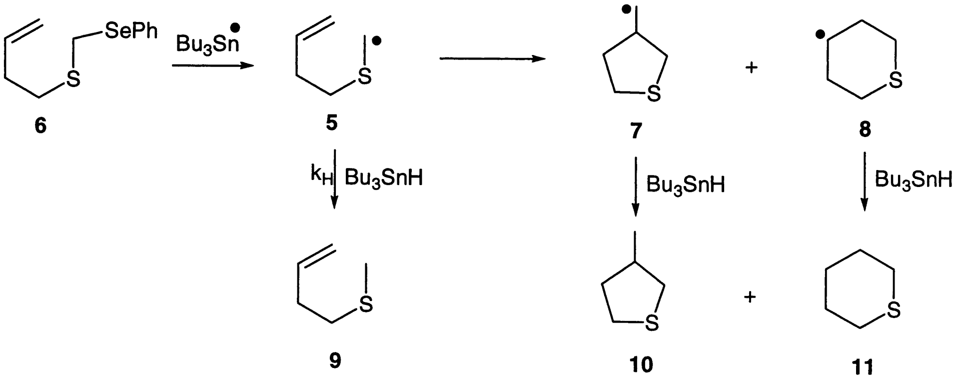
We recently initiated a study of the analogous sulfur-containing radical **5**. Calculations[4] predict that sulfur and oxygen have essentially the same stabilising effect on an adjacent radical centre and we felt confident that, on this basis at least, the radical **5** would show the same tendency to cyclise as **1** (X = O). The aspects of interest to us were: (i) the effect of the longer C–S bond lengths on the facility for ring closure of the 2-thia-5-hexenyl radical **5**, and (ii) the regiochemistry of reaction if cyclisation were a viable process (Scheme 1).



Scheme 1.

The selenide **6**, selected as precursor to **5**, was synthesised by application of standard procedures. A 0.013 M solution of **6** in benzene was heated to 80°C and treated dropwise over 10 minutes with a solution of Bu_3SnH (1.2 equiv.) in benzene containing 1 mol% of AIBN as an initiator. After a further 2 hours at 80°C, the mixture was cooled and quenched with carbon tetrachloride. GC analysis of the product revealed the presence of the sulfides **9**, **10** and **11** in the ratio 17:70:13 (Table 1).

Table 1
Distribution of acyclic and cyclised products from reduction of the selenides **6** and **13** in benzene with tributyltin hydride

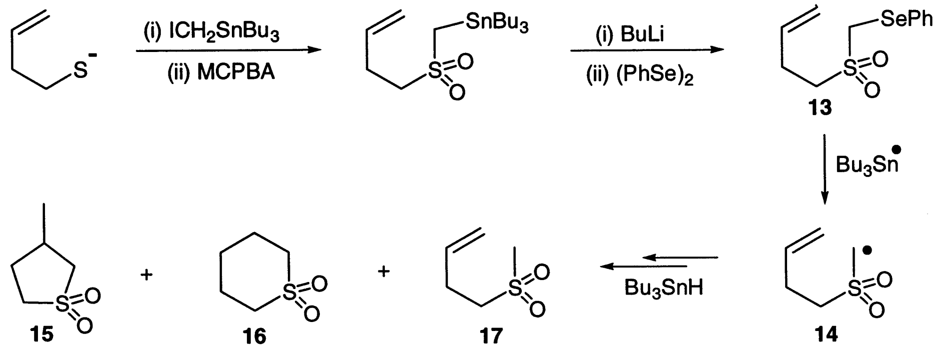
Substrate	Radical	[Conc.][a] (M)	Temp (°C)	Product distribution[b]		
				Reduced	5-*exo*	6-*endo*
6	**5**	0.013	80	17.1	70.1	12.8
6	**5**	0.052	80	33.1	56.6	10.3
13	**14**	0.013	80	3.8	73.1	23.1
13	**14**	0.052	80	8.9	69.6	21.5

[a] Concentration of substrate.
[b] $(Bu_3Sn)_2O$ added to remove adventitious PhSeH.[8]

It is seen that, in contrast to the behaviour of the oxa and ammonium radicals **1** (X = O, Me_2N^+), **5** leads to a relatively large proportion (ca 15%) of acyclic (reduced) product as well as a significant quantity (ca 13%) of the isomer formed via 6-*endo* closure. These observations are a reflection of an attenuated stereoelectronic effect; we attribute the greater difficulty experienced by **5** in attaining the transition state associated with the usual 5-*exo* mode of ring closure to the effect of the longer C–S bonds. Significantly, Wilt[5] has observed that the corresponding α-silyl radical **1** (X = $SiMe_2$) gives only a very small amount of cyclised material (5-*exo*:6-*endo* =

1:2) and has attributed this to the effect of the longer C–Si bonds. Another factor which may contribute, and warrants further study, is the possibility of an enhanced rate of hydrogen abstraction (k_H) from Bu_3SnH by **5**.

For comparison, we have also examined the behaviour of the 2-sulfonyl-5-hexenyl radical **14**. Unlike the highly nucleophilic parent species **5**, the radical **14** possesses considerable electrophilic character.[6] The precursor of choice, **13**, was synthesised as illustrated in Scheme 2.



Scheme 2.

Exposure of the sulfone **13** in benzene to Bu_3SnH (1.2 equiv.) under the conditions described above afforded a 73:23 mixture of the cyclic sulfones **15** and **16** (combined GC yield: 96%) accompanied by a small quantity of the acyclic product **17** (<4%). The small amount of reduced product detected is consistent with an enhanced reactivity of the α-sulfonyl radical **14** towards cyclisation. Interestingly, the rate of ring closure in this case does not appear to be affected significantly by the long C–S bonds. Calculations[7] predict that, in contrast to the effect of an α-thia group, the presence of a sulfonyl group α to the radical centre is not energetically favourable. Evidently, the increased ground state energy of radical **14** leads to a reduced activation energy for its ring closure compared with that of **5**. Furthermore, in view of the different nucleophilic/electrophilic properties of the radicals **5** and **14**, the relative proportion of *endo* ring closure in the two types of radicals may be attributed to a different mix of SOMO and LUMO/HOMO frontier orbitals in the transition state for ring closure of **14** relative to those in **5**.

The observation that the ratio of the heterocycles produced in each of the cyclisation processes **5**→**7**+**8** and **14**→**15**+**16** remains constant with changes in the concentration and rate of addition of Bu_3SnH indicates that these reactions occur irreversibly.

We plan to extend the investigation to include a study of the corresponding sulfinyl and sulfonium-substituted radicals **1** (X = SO, MeS^+), as well as a determination of the rates of cyclisation of the radicals **5**, **14** and **1** (X = SO, MeS^+).

Acknowledgements

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References

1. (a) Beckwith, A. L. J.; Glover, S. A. *Aust. J. Chem.* **1987**, *40*, 157. (b) Rawal, H. R.; Singh, S. P.; Dufour, C.; Michoud, C. *J. Org. Chem.* **1993**, *58*, 7718.
2. Padwa, A.; Nimmersgen, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620.
3. (a) Della, E. W.; Knill, A. M.; Smith, P. A. *Chem. Commun.* **1996**, 1637. (b) Della, E. W.; Smith, P. A. *J. Org. Chem.* **1999**, *64*, 1798.
4. (a) Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062. (b) Bordwell, F. G.; Zhang, X.-M.; Alnajjar, M. S. *J. Am. Chem. Soc.* **1992**, *114*, 7623. (c) Della, E. W.; Graney, S. D. unpublished data.
5. Wilt, J. W. *Tetrahedron* **1985**, *41*, 3979.
6. An indication of the electrophilic nature of the α-substituted radical **14** relative to that of **5** is provided by a comparison of the σ_p values of the substituents: $\sigma_p(SMe)=0.0$; $\sigma_p(SO_2Me)=0.7$ (Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165).
7. Della, E. W.; Graney, S. D.; Schiesser, C. H. unpublished data.
8. Maxwell, B. J.; Smith, B. J.; Tsanaktsidis, J. *J. Chem. Soc., Perkin Trans. 2* **2000**, 425–431.