Tetrahedron Letters, Vol. 34, No. 7, pp. 1219-1222, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

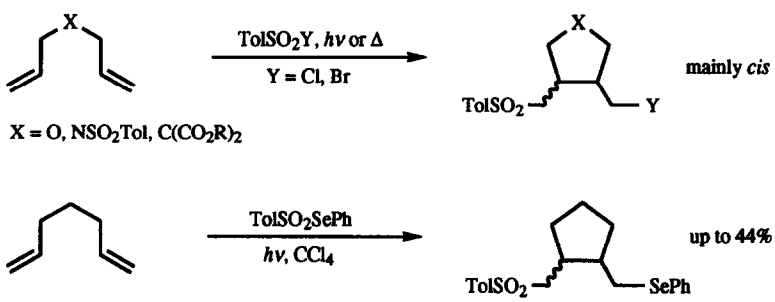
Radical Cyclisation of Dienes and Enynes using $TolSO_2SePh$

Julie E. Brumwell and Nigel S. Simpkins*
Department of Chemistry, University of Nottingham, University Park, Nottingham NG7 2RD, UK

and Nicholas K. Terrett
Pfizer Central Research, Sandwich, Kent CT13 9NJ, UK

Abstract: Reaction of a number of 1,6-diene or enyne systems with $TolSO_2SePh$, under free radical conditions, results in selenosulphonylation with concommitant C–C bond formation, to give cyclised alkyl or vinyl sulphones containing the synthetically useful phenylselenyl functionality.

The use of carbon-centred radicals in organic synthesis has become widespread in recent years, as the value of radical reactions, particularly for ring formation, has been properly recognised.[1] One area of radical cyclisation chemistry which attracted our attention involves the reaction of simple 1,6-dienes or enynes with a range of sulphonyl compounds $ArSO_2Y$ (Y = Cl or Br), which results in overall halosulphonylation with concommitant C–C bond formation, Scheme 1.[2]

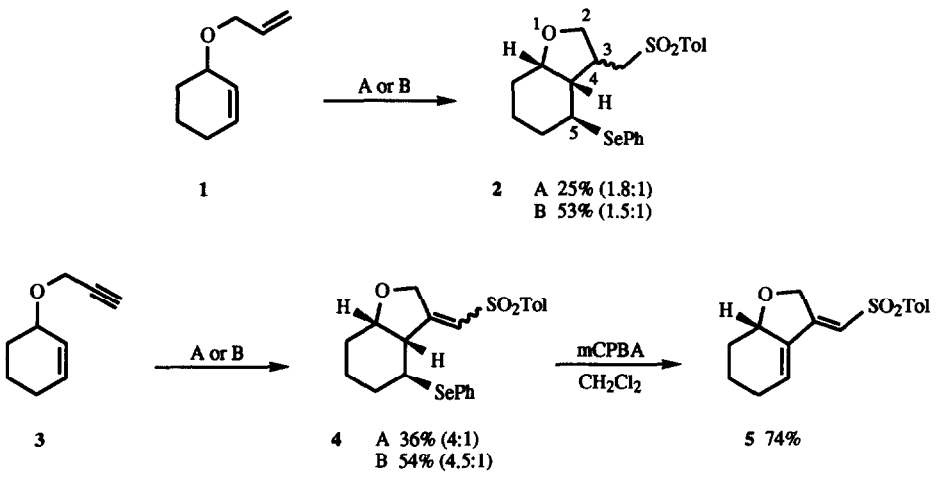


Scheme 1

This reaction is appealing, because in one simple step, useful functionality is introduced, a new C–C bond is formed (usually stereoselectively) and two unsaturated appendages with similar, or identical, reactivity are distinguished. The chemistry is usually most successful with sulphonyl bromides, since in this case the radical chain transfer step is of a rate appropriate to allow cyclisation of the initially formed carbon-centred radical (with sulphonyl iodides the chain transfer step is usually too rapid to allow efficient cyclisation, whereas the use of sulphonyl chlorides usually requires special conditions such as the inclusion of copper salts).

As shown, Kang and Kice have also reported a single example of a cyclisation using a selenosulphonate, i.e. $TolSO_2SePh$, although here the chain transfer step was considered too rapid to render the reactions synthetically useful.[3] Here we show that the free radical selenosulphonylation–cyclisation is a generally useful process for the preparation of a range of five-membered selenosulphone products in good to excellent yield.

In previous work, free radical halosulphonylation has been conducted under either photolytic or thermal reaction conditions. We examined both types of conditions with the simple diene and enyne substrates **1** and **3**, respectively, Scheme 2.[4]



1 **2** A 25% (1.8:1) B 53% (1.5:1)

3 **4** A 36% (4:1) B 54% (4.5:1) **5** 74%

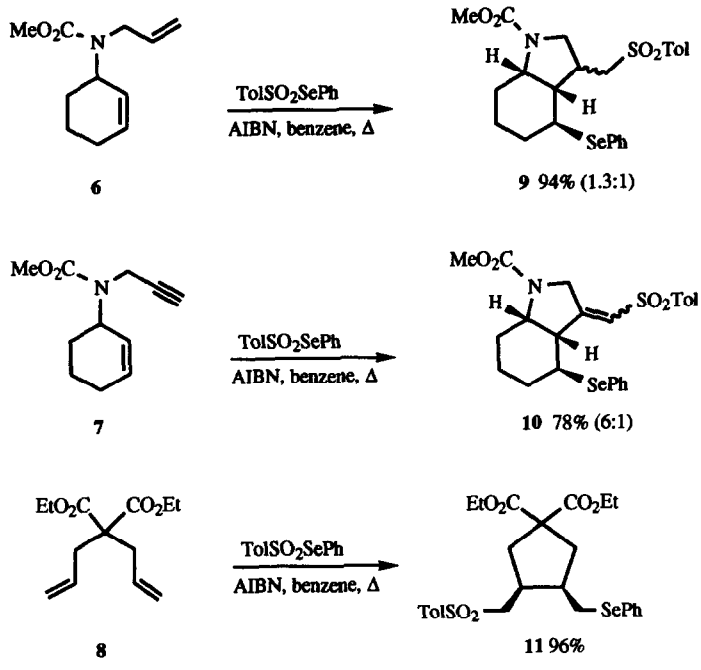
A - *hν* (300W tungsten filament), $CHCl_3$
B - AIBN in benzene at reflux

Scheme 2

With both types of substrate the yield of the desired cyclised product, **2** or **4**, was significantly better when the reaction was conducted under thermal conditions, in the presence of AIBN, than under photolytic conditions. In the case of **2** we obtained two products, epimeric at C-3, indicating that high stereoselectivity at C-5 is observed, presumably due to radical chain transfer on the *exo*-face of the concave bicyclic system.[5]

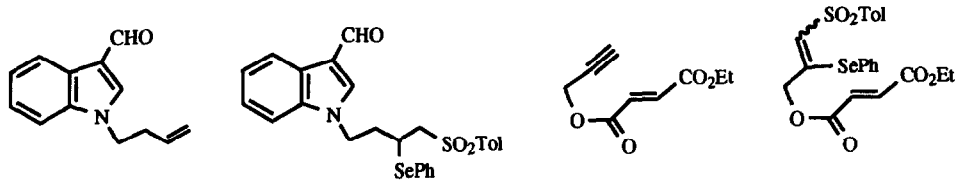
Two stereoisomeric products are also formed in the case of **4**, these being double bond isomers with the *Z*-alkene predominating. Treatment of **4** with mCPBA in CH_2Cl_2 resulted in clean selenoxide formation and *in situ syn*-elimination to give the dienyl sulphone **5**, thus illustrating one application of this chemistry to the rapid synthesis of bicyclic sulphonyl dienes, which are useful in reverse electron demand cycloadditions.[6]

The generality of the radical cyclisation procedure was next examined, by reacting the substrates **6**, **7** and **8** under the thermal conditions used for **1** and **3**, Scheme 3. Each of these reactions gave the desired cyclised products in excellent yield, with **9** and **10** being formed as mixtures of isomers, whereas in the case of **8** we were able to detect only one isomeric product, presumably the *cis*-substituted cyclopentane product **11**.[7]



Scheme 3

However, the reaction fails in the case of indole **12**, in which cyclisation onto the rather electron-rich vinylogous amide system would be required,[8] and also fails for **14**.[9] In both cases the major product isolated is that resulting from addition of $TolSO_2SePh$ to the unsaturated side chain, to give **13** and **15**.



12 **13** **14** **15**

The $TolSO_2SePh$ radical cyclisation protocol displays many features in common with the corresponding $TolSO_2Br$ reactions and may be limited to substrates capable of rapid 5-*exo* cyclisation. However, the examples shown in Schemes 2 and 3 clearly indicate the utility of this approach for the synthesis of certain types of functionalised and unsaturated sulphones.

Acknowledgements

We are grateful to the Science and Engineering Research Council and Pfizer Central Research, Sandwich, Kent CT13 9NJ, UK for support of JEB under the CASE scheme.

References

1. (a) Geise, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon Press: Oxford, 1986; (b) Regitz, M.; Geise, B. Eds. *Methoden Der Organischen Chemie (Houben-Weyl)*; Thieme: Stuttgart, 1989; Vol. E19a; (c) Curran, D. P. *Synthesis* **1988**, 417 and 489; (d) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541.
2. (a) De Riggi, I.; Surzur, J-M.; Bertrand, M. P. *Tetrahedron* **1988**, *44*, 7119; (b) Chuang, C-P.; Ngoi, T. H. J. *Tetrahedron Lett.* **1989**, *30*, 6369; (c) Serra, A. C.; da Silva Correa, C. M. M.; Vieira, M. A. M. S. A.; Gomes, M. A. *Tetrahedron* **1990**, *46*, 3061; (d) De Riggi, I.; Surzur, J-M.; Bertrand, M. P.; Archavlis, A.; Faure, R. *Tetrahedron* **1990**, *46*, 5285; (e) Serra, A. C.; da Silva Correa, C. M. M.; do Vale, M. L. C. *Tetrahedron* **1991**, *47*, 9463; (f) Chuang, C-P. *Tetrahedron Lett.* **1992**, *33*, 6311.
3. Kang, Y-H.; Kice, J. L. *J. Org. Chem.* **1984**, *49*, 1507.
4. Typical experimental conditions involve heating a solution of the starting diene or enyne (*ca.* 0.08M) in benzene under reflux, in the presence of $TolSO_2SePh$ (1 eq.) and AIBN (0.1 eq.), under an atmosphere of dry nitrogen. When reaction is complete (as monitored by TLC, typically 5–8h) the solvent is removed under reduced pressure, and the residue subjected to column chromatography to give the pure sulphone product.
5. We have assigned compounds **2** and **9** as epimeric at C-3 rather than C-5, based on our studies of the corresponding $TolSO_2Br$ adducts, which are formed as analogous epimeric mixtures. Thus in the case of the epimeric bromides corresponding to selenide **2**, treatment with Bu_3SnH gives a debrominated sulphone, *also as a mixture of epimers* - clearly indicating that the initial adducts are epimeric at C-3.
6. For a comprehensive review of this area, including dienyl sulphone preparation and cycloadditions, see Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993.
7. The assignment of vinyl sulphone stereochemistry for the major isomer of **4** and **10** is based on the expectation that the initially formed *Z*-vinyl radical should cyclise much faster than the *E*-form. This assignment is also in accord with chemical shifts seen in the ^1H NMR spectra for the allylic protons, which show a characteristic downfield shift if *cis* to the SO_2Tol group. The assignment of the *cis* substitution pattern in **11** is based on ample literature precedent, e.g. Reference 2.
   Selected data for sulphone products (*J* values in Hz): **4** (major isomer) (Found: C, 59.07; H, 5.46. $C_{22}H_{24}O_3SSe$ requires C, 59.06; H, 5.41%); ν_{max} ($CHCl_3$)/cm^{-1} 2945, 2855, 1645, 1598, 1303, 1146, 1088 and 962; δ_H (250 MHz, $CDCl_3$) 1.45–1.56 (4H, m), 1.92–2.09 (2H, m), 2.43 (3H, s, C_6H_4*Me*), 2.60 (1H, dd, *J* 10 and 4.2, C=C–C*H*), 2.89 (1H, m, C*H*SePh), 3.95 (1H, m, C*H*OCH_2), 4.80 (1H, dd, *J* 17.5 and 2.6, OCH_2C=C), 5.04 (1H, d, *J* 17.5, OCH_2C=C), 6.66 (1H, br.s, C=C*H*), 7.17–7.43 (7H, m, Ar) and 7.78 (2H, d, *J* 8.3, Ar); δ_C (67.8 MHz, $CDCl_3$) 20.92 (t), 21.60 (q), 26.70 (t), 33.46 (t), 43.60 (d), 49.99 (d), 68.84 (t), 77.27 (d), 123.15 (d), 127.13 (d), 127.67 (s), 128.05 (d), 129.02 (d), 129.88 (d), 135.53 (d), 138.53 (s), 144.35 (s) and 159.34 (s); *m/z* (FAB) 448 (M^+-1, 24%), 291 (38), 154 (100), 136 (84), 107 (40), 91 (61), 77 (57) and 63 (29). **5** (Found: C, 66.28; H, 6.39. $C_{16}H_{18}O_3S$ requires C, 66.18; H, 6.25%). **9** (Found: C, 56.85; H, 5.85; N, 2.65. $C_{24}H_{29}NO_4SSe$ requires C, 56.91; H, 5.77; N, 2.77%). **10** (Found: C, 57.12; H, 5.64; N, 3.00. $C_{24}H_{27}NO_4SSe$ requires C, 57.14; H, 5.39; N, 2.78%). **11** ν_{max} (film)/cm^{-1} 2981, 1728, 1478, 1439, 1302, 1261, 1182, 1148 and 1089; δ_H (250 MHz, $CDCl_3$) 1.21 (3H, t, *J* 7), 1.23 (3H, t, *J* 7), 1.95–2.91 (8H, m), 2.42 (3H, s, C_6H_4*Me*), 2.97–3.31 (2H, m, CH_2SO_2Tol), 4.15 (2H, q, *J* 7), 4.16 (2H, q, *J* 7), 7.21–7.45 (7H, m, Ar) and 7.76 (2H, d, *J* 8.2).
8. For previous cyclisations of related vinylogous amides, see Middleton, D. S.; Simpkins, N. S.; Terrett, N. K. *Tetrahedron Lett.* **1989**, *30*, 3865.
9. This is to be expected considering the findings of Serra *et al.*, see Reference 2(e).

(Received in UK 16 November 1992)