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Demonstration of Reversible C-C Bond Cleavage in Oxiranylcarbinyl Radicals.

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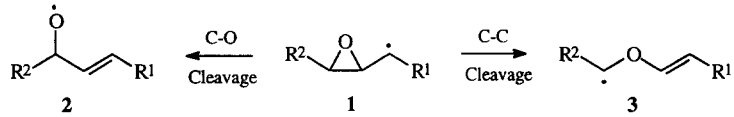
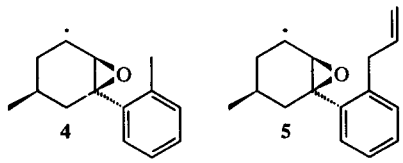
Abstract: The incorporation of a stereochemical probe into aryl substituted oxiranylcarbinyl radicals has demonstrated that the C-C bond cleavage in these systems is reversible, and that it can occur even when no products of C-C cleavage are obtained. © 1997 Elsevier Science Ltd.

There is kinetic,[1] and other evidence,[2-4] that oxiranylcarbinyl radicals **1** undergo rapid and reversible C-O bond cleavage to give **2**. Products derived from C-C bond cleavage have been reported[5-8] when the resultant carbon centred radical **3** is stabilised (R_2 = aryl, vinyl or acyl) and it has been suggested[1] that the reactions may be thermodynamically controlled under certain conditions (see Scheme 1).



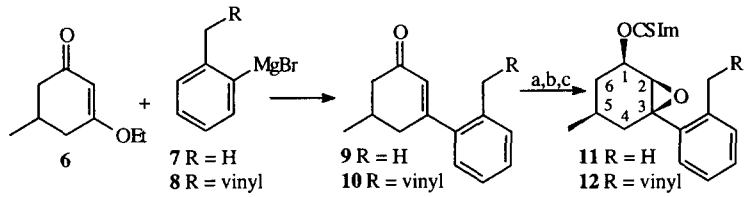
Scheme 1

As part of our ongoing investigations into factors controlling β-cleavage and the synthetic applications of oxiranylcarbinyl radicals,[6,9] we have examined the reactions of the radicals **4** and **5** and now report the first direct stereochemical evidence for the reversibility of the C-C cleavage.



The radicals **4** and **5** were generated from the thiocarbonylimidazolides **11** and **12**, prepared as single diastereomers as shown in Scheme 2. The *cis* diequatorial relationship between the Me group and the OCSIm group was apparent from the spin-spin coupling constants in which the axial proton at C-6 clearly showed two large (11.5 Hz) axial-axial couplings to the protons at C-1 and C-5. This assignment was also supported by the observation of an nOe effect between the C-1 and C-5 protons. The epoxide function is presumed to be *cis*

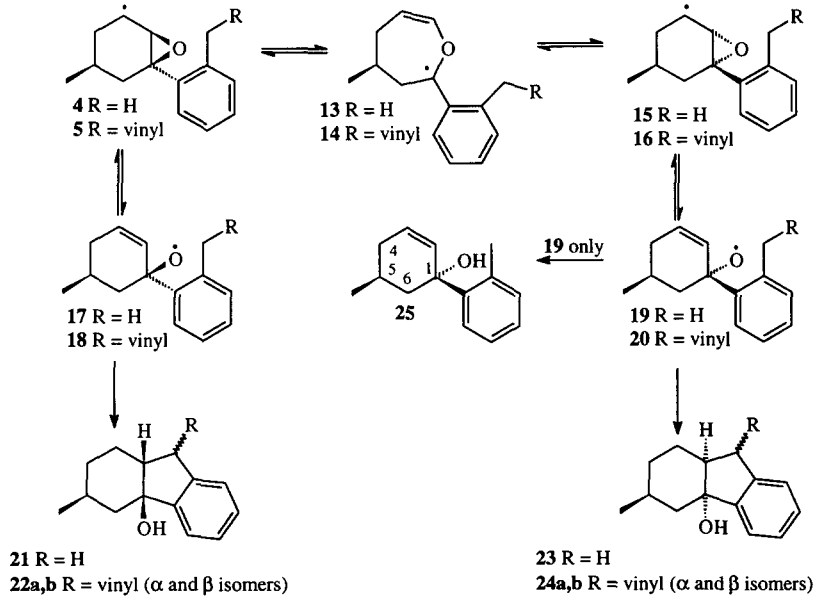
owing to the directing influence of the OH group in the epoxidation of allylic alcohols,[10] and is consistent with that observed in closely related examples.[6,11]



a) $NaBH_4$, $CeCl_3$, MeOH, 0°C. b) *m*CPBA, Na_2CO_3, DCM, 0°C. c) $CS(Im)_2$, DCM, reflux.

Scheme 2

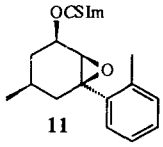
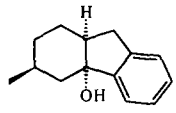
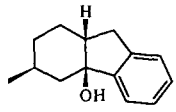
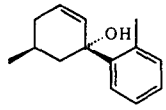
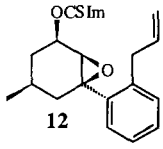
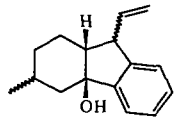
The products of the reactions of the thiocarbonylimidazolides **11** and **12** with Bu_3SnH/AIBN (see Table) are all derived from C-O cleavage and are largely analogous to those reported by Rawal,[11] in related reactions. However, the incorporation of the cyclohexane ring methyl group as a stereochemical probe and the aryl ring to facilitate C-C bond cleavage provides significant insight into the reaction mechanism (see Scheme 3).



Scheme 3

The isolation of the diastereomeric fluorenols **21** and **23** and the alcohol **25** from **11** and the four diastereomeric fluorenols **22a**, **22b**, **24a** and **24b** from **12** is best explained by a reversible cleavage of the C-C bond. Particularly noteworthy is the relatively high yield under conditions of inverse addition of the alcohol **25** in which the relative configuration of the oxygen and the methyl group is reversed from that in the starting material **11**. The failure to observe products of reduction of the first formed alkoxy radical **17** and the benzylic radicals **13**, **14** is ascribed to steric hindrance.

Table : Results of Bu_3SnH/AIBN reactions on thiocarbonylimidazolides **11** and **12**

Substrate	Products	Isolated Yield (%) (Normal Addition)[a]	Isolated Yield (%) (Inverse Addition)[b]
 **11**	 **23**	14[c]	0
	 **21**	18	0
	 **25**	21[d]	59
 **12**	 **22a,b + 24a,b**	37[e]	36

[a]4 Hour addition of Bu_3SnH (1.4 eq) and AIBN (0.1 eq) to the substrate in refluxing benzene

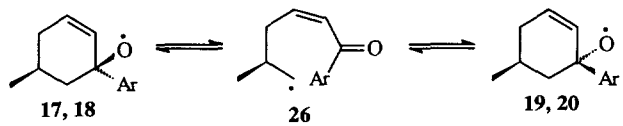
[b]4 Hour addition of the substrate and AIBN (0.1 eq) to Bu_3SnH (1.4 eq) in refluxing benzene.

[c] Stereochemistry assigned from X-ray analysis.[12]

[d] Stereochemistry assigned from ^1H NMR coupling constants.[13]

[e]4 Diastereomers (Ratio 14:53:29:4 by GCMS)

An alternative explanation for the epimerisation of the epoxides is the reversible β-cleavage of the alkoxy radicals **17, 18** (see Scheme 4). This is thought to be less likely since the formation of the primary radical **26** is unfavourable energetically,[14] and might be expected to lead to alternative products.[11(a)]



17, 18 **26** **19, 20**

Scheme 4

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References and Notes

1. Ziegler, F. E.; Peterson A. K. *J. Org. Chem.*, **1995**, *60*, 2666-2667.
2. Nussbaum, A. L.; Wayne, R.; Yuan, E.; Zagneetko, O.; Oliveto, E. P. *J. Am. Chem. Soc.*, **1962**, *84*, 1070-1071.
3. Weinberg, J. S.; Miller, A. *J. Org. Chem.*, **1979**, *44*, 4722-4725.
4. (a) Suginome, H.; Wang, J. B. *J. Chem. Soc., Chem. Commun.*, **1990**, 1629-1631. (b) Galatsis, P.; Millan, S. D. *Tetrahedron Lett.*, **1991**, *32*, 7493-7496. (c) Rawal, V. H.; Iwasa, S. *Tetrahedron Lett.*, **1992**, *33*, 4687-4690. (d) Galatsis, P.; Millan, S. D.; Faber, T. *J. Org. Chem.*, **1993**, *58*, 1215-1220.
5. Stogryn, E. L.; Gianni, M. H. *Tetrahedron Lett.*, **1970**, 3025-3028.
6. Corser, D. A.; Marples, B. A.; Dart, R. K. *Synlett*, **1992**, 987-989.
7. Murphy, J. A.; Patterson, C. W. *J. Chem. Soc. Perkin Trans. 1*, **1993**, 405-410.
8. Breen, A. P.; Murphy, J. A.; Patterson, C. W.; Wooster, N. F. *Tetrahedron*, **1993**, *49*, 10643-10654.
9. Bowman, W. R.; Brown, D. S.; Burns, C. A.; Marples, B. A.; Zaidi, N. A. *Tetrahedron*, **1992**, *48*, 6883-6896.
10 Henbest, H. B.; Wilson, R. A. L. *J. Chem. Soc.*, **1957**, 1958-1965
11. (a) Rawal, V. H.; Newton, R. C.; Krishnamurphy V. *J. Org. Chem.*, **1990**, *55*, 5181-5183. (b) Rawal, V. H.; Krishnamurphy, V. *Tetrahedron Lett.*, **1992**, *33*, 3439-3442. (c) Rawal, V. H.; Krishnamurphy, V.; Fabre, A. *Tetrahedron Lett.*, **1993**, *34*, 2899-2902.
12. The X-ray crystallographic data for **23** have been deposited at the Cambridge Crystallogaphic Database.
13. The *o*-tolyl group in **25** was assumed to adopt a pseudo-equatorial conformation because of its steric bulk. The spin-spin coupling constants between the axial protons at C-4 and C-6 and the proton at C-5 (10 and 12 Hz respectively) suggest that the methyl group is equatorial.
14. Laird, E. R.; Jorgensen, W. L. *J. Org. Chem.*, **1990**, *55*, 9-27.

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