A Novel Probe for Free-radical Intermediates

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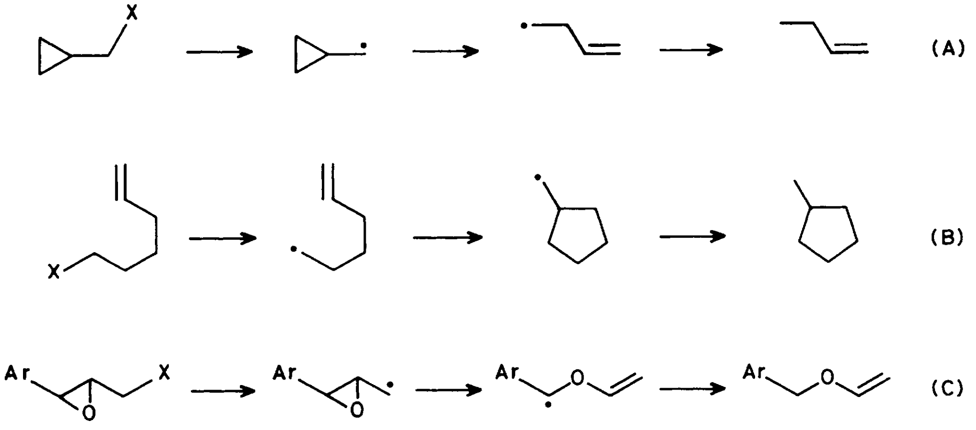
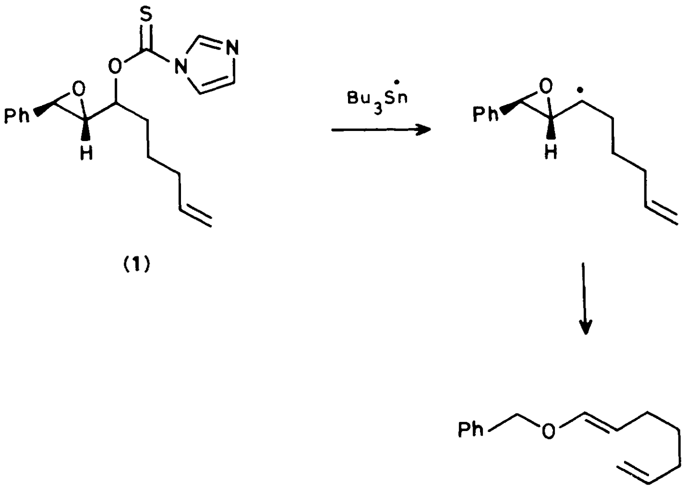
C–C bond cleavage of oxiranes, which is triggered by adjacent homolysis but not heterolysis, occurs at a sufficiently rapid rate to be a useful probe for free-radical intermediates in chemical and biological systems.

The utility of reactions which detect radical intermediates in chemistry has been explored recently. Two classes of probe have seen common usage; these feature cyclopropane cleavage[1] [reaction (A) in Scheme 1] and cyclopentane formation[2] [reaction (B)]. Beckwith[3] has studied the reactions of cyclopropylmethyl *anions* and Garst[4] has studied the reactions of *anionic* equivalents of reaction type (B) and both have found that the anions perform similar chemistry to the radicals. So these systems are not ideal for unambiguously indicating radicals as intermediates. We needed to be able to distinguish radical from anionic intermediates in a number of reactions we are studying, and so, wished to develop a probe which would positively indicate the presence of radicals by a reaction which could not be brought about by the corresponding anion. One candidate reaction is C–C bond cleavage in certain epoxides[5] [reaction (C)], but to be useful it was necessary to demonstrate that this reaction occurred at an acceptably rapid rate and that heterolytic cleavage did not produce the same result.

We have demonstrated through a competition experiment that epoxide opening occurs faster than reaction type (B). The epoxide (**1**) was synthesised[6] and cleaved by tributylstannyl radicals, to leave the vinyl ether (**2**) as a mixture of *E*- and *Z*-isomers in 54% isolated yield. No cyclopentane (or cyclohexane) derivative was observed.[7] This implies that the epoxide cleavage occurs faster than cyclopentane formation, and hence occurs at a sufficiently rapid rate to be useful for detection of radical intermediates.

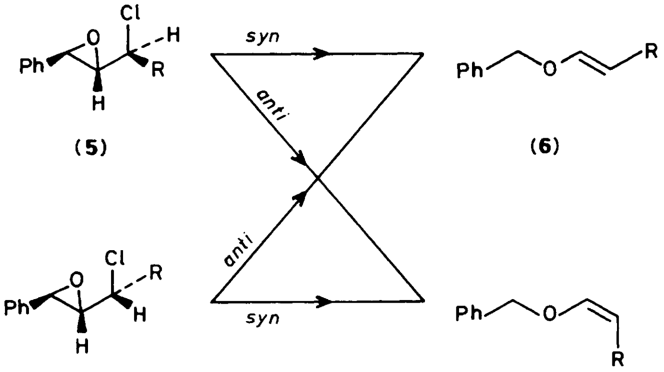


Scheme 1

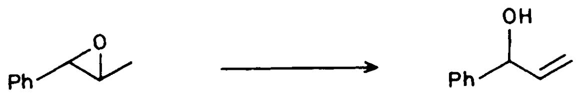


(1)

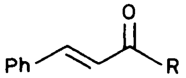
(2)



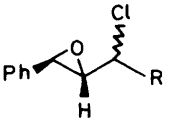
(5) (6) (7) (8)



(9) (10)



(3a) R = Ph
(3b) R = Me



(4a) R = Ph
(4b) R = Me

The epoxide cleavage reactions (C) could occur by concerted C–X and C–C bond cleavages, without the formation of an intermediate free radical. For our purpose, we wished to show that this type of reaction could be triggered by a true free radical fomed adjacent to the epoxide. To this end the enones (**3**) were converted into the corresponding chloro-epoxides (**4**). Both chloro-epoxides were produced as a mixture of diastereoisomers about the chlorine-bearing carbon with one of the diastereoisomers being isolated in much greater yields than the other. This major diastereoisomer was in each case cleaved with tributylstannyl radicals. The major diastereoisomer can be represented by (**5**) or (**7**), but we cannot say which. If C–Cl and C–C bond cleavage is concerted, then if our diastereoisomer is (**5**) we should expect production of solely (**6**) or solely (**8**) as shown depending on whether the C–Cl and C–C bonds lined up synperiplanar or antiperiplanar respectively. We are not aware of precedent which would allow us to be certain which of these two orientations is favoured. Similarly if our diastereoisomer is (**7**) we should expect production solely of (**8**) for synperiplanar orientation or of (**6**) for antiperiplanar. The important point to note is that concerted reaction should produce one vinyl ether stereoisomer from a single diastereoisomer of chloro-epoxide. In both the cleavage reactions we performed we obtained a 1 : 1 mixture of (**6**) and (**8**). This loss of stereochemical integrity during the reaction implies the existence of a free radical on the carbon adjacent to the epoxide.

Finally, we treated the epoxide (**9**) with lithium di-isopropylamide to give the allylic alcohol (**10**) as major product. No trace of vinyl ether was formed as expected from literature precedent.

This work shows therefore that where carbon–carbon bond cleavage occurs in epoxides, this is consistent with radical-induced and not with anion-induced cleavage. Such epoxides cleave at a suitably rapid rate to make them useful probes for radicals in organic reactions.

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