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Radical-Induced Cleavages in Ring-Fused Epoxides.

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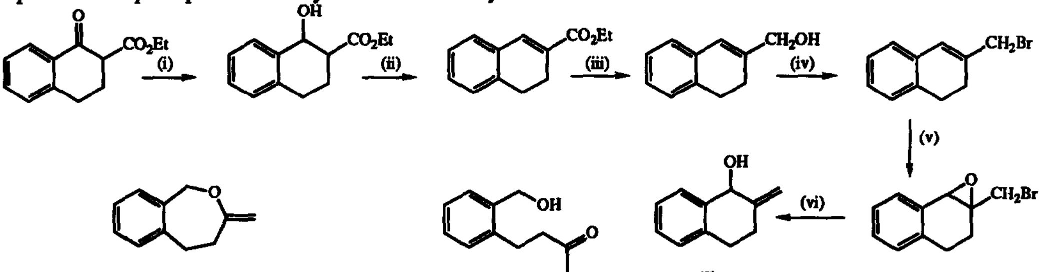
Abstract. Carbon-carbon bond cleavage has been observed in ring-fused epoxides where stereoelctronic effects do not interfere.

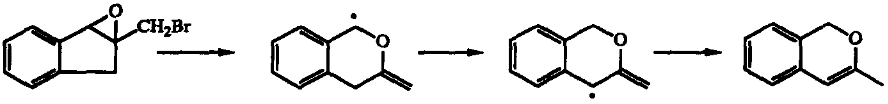
The cleavage of epoxides by radical chemistry has been a subject of growing mechanistic and synthetic interest. Both carbon-oxygen[1,2] and carbon-carbon bond cleavage have been noted, with the former predominating. Carbon-carbon bond cleavage has only been observed in aryl epoxides,[3b,d,e] in vinyl epoxides[3a] and in ketoepoxides[3c], suggesting that a π-system adjacent to the site of the developing radical is important for this reaction. With one exception[4], the examples of C-C bond cleavage which have been seen are from epoxides derived from acyclic alkenes. Interest in extending the utility of radical reactions of epoxides has prompted this study of their chemistry.



(4) (3) (2) (1)

(i) NaBH$_4$, EtOH, (51%) (ii) pTSA, (94%) (iii) iBu$_2$AlH (91%), (iv)Me$_2$S, NBS CH$_2$Cl$_2$ (87%), (v) mCPBA (92%), (vi) Bu$_3$SnH, AIBN, PhH.

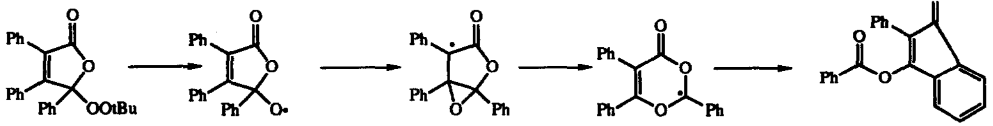
The epoxybromide (1) was prepared as shown from tetralone. Treatment of this molecule with tributyltin hydride and AIBN initiator led to the isolation of the allylic alcohol (2) (21%), a product of C-O bond cleavage, and the hydroxyketone (3) (35%). The latter must result from C-C cleavage, quenching of the resulting radical with tributyltin hydride to give oxepane (4), and hydrolysis of the vinyl ether on silica. Attempts to isolate the oxepane were not successful even when the reaction products were chromatographed on silica which had been doped with 2% w/w potassium carbonate.



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

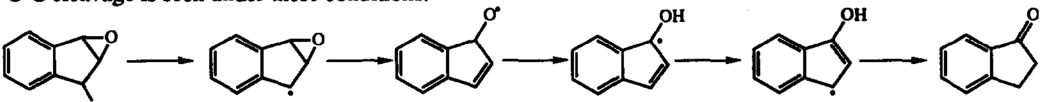
The bromoepoxide (5) was similarly prepared from indanone. Radical activation of this compound as before yielded only one product following chromatography, which was surprisingly the chromene (8) (27%). This arose as a result of carbon-carbon bond cleavage to give the radical (6), which isomerised presumably by an intermolecular reaction to the isomeric radical (7). Quenching of (7) then led to the observed chromene.

In the above cases, the radical produced on cleavage of the halogen atom is exocyclic and has freedom to orient itself parallel to the σ* orbital of either the C-O or the C-C bonds. The case where the radical is conformationally constrained provides a more interesting study. It is known that in epoxides[2] (without adjacent π-systems) derived from steroids, stereoelectronic restrictions lead to cleavage of the exocyclic (C-O) bond of the epoxide. However, homolysis of the peroxide (9) at 115-120°C has been shown[4] to lead to the indanone (11), and it has been suggested that this results from the pathway shown. Here, the constrained radical (10) causes C-C bond cleavage contrary to the stereoelectronic bias but giving the thermodynamically more stable radical. It is possible that C-O bond cleavage of epoxy radicals like (10) occurs, but that the process is reversible, and that in the absence of sources of hydrogen atoms acting as quenching agents, that C-C cleavage ultimately occurs.(The reversibility of such reactions has yet to be established) Can similar epoxide openings under our lower temperature conditions (80°C) produce thermodynamic products? This would obviously depend on the kinetics of the reversal[5] of the C-O cleavage reaction, the size of the stereoelectronic effects, and the rates of abstraction of hydrogen from tributyltin hydride by the carbon- and oxygen-centred radicals involved.



(9) (10) (11)

The indane epoxy bromide (12) was prepared from trimethylsilylindene[6]. Treatment with tributyltin hydride and AIBN gave only one product after chromatography, - indanone. This results from C-O cleavage to (13), radical isomerisation to (14) and hydrogen atom abstraction from tributyltin hydride. No C-C cleavage is seen under these conditions.



(12) (13) (14)

In summary, carbon-carbon bond cleavage is observed in ring-fused epoxides, but at the temperature of refluxing benzene, stereoelectronic effects can prevent this in cases where the initial radical has restricted conformational mobility.

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