

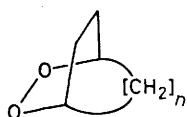
## A General Route to Dioxabicyclo[*n*.2.1]alkanes

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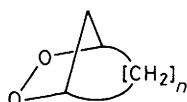
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6,7-Dioxabicyclo[3.2.1]octane has been prepared from its *cis*-8-bromo derivative by reduction with tributyltin hydride generated *in situ* from bis(tributyltin) oxide and polymethylhydrogen siloxane; analogous reactions have afforded 7,8-dioxabicyclo[4.2.1]nonane and 8,9-dioxabicyclo[5.2.1]decane.

Saturated bicyclic peroxides that contain either a 5- or a 6-membered peroxide ring are of interest because they are homologues of 2,3-dioxabicyclo[2.2.1]heptane, the reactive bicyclic peroxide skeleton in prostaglandin endoperoxides.<sup>1</sup> Three simple dioxabicyclo[*n*.2.2]alkanes (1) (*n* = 2–4) are known and each was prepared by singlet oxygenation of the appropriate cycloalka-1,3-diene followed by reduction with di-imide.<sup>2</sup> In contrast no general route exists for the synthesis



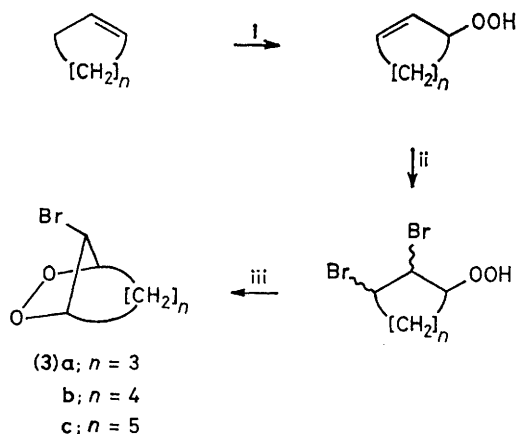
(1)



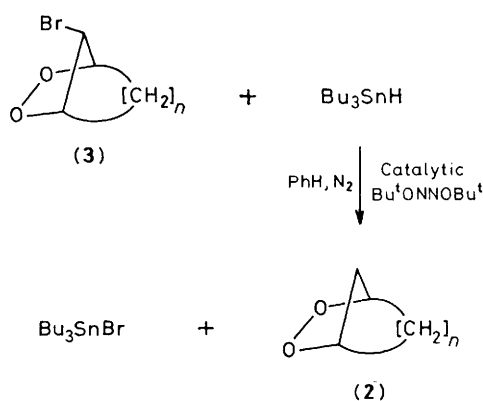
(2) a; *n* = 3  
b; *n* = 4  
c; *n* = 5

of dioxabicyclo[*n*.2.1]alkanes (2). We have prepared 8,9-dioxabicyclo[5.2.1]decane (2c) by peroxymercuration of cyclo-octa-1,4-diene followed by reduction with sodium borohydride, but the method was unsuccessful with cyclohexa-1,4-diene.<sup>3</sup> Adam<sup>4</sup> has obtained 7,8-dioxabicyclo[4.2.1]nonane (2b) by di-imide reduction of the corresponding nona-2,4-diene; this is one of the three endoperoxides afforded by singlet oxygenation of cyclohepta-1,3,5-triene. Although 8-bromo,<sup>5</sup> 2-bromo,<sup>6</sup> 2,4-dibromo,<sup>3</sup> and 1,5-dimethyl<sup>7</sup> derivatives of 6,7-dioxabicyclo[3.2.1]octane have been prepared, the parent compound (2a) remains unreported. We now describe a general method for the preparation of dioxabicyclo[*n*.2.1]alkanes (2) (*n* = 3–5), which not only yields the elusive [3.2.1]-peroxide, but also represents a more convenient route to the [4.2.1]-compound.

The method involves reductive debromination of *cis*-(*n* + 5)-bromodioxabicyclo[*n*.2.1]alkanes (3), which are readily prepared from cycloalkenes by the simple sequence of reactions

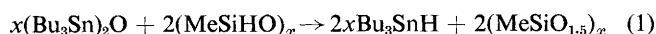


Scheme 1. Reagents: i,  $^1\text{O}_2$ ; ii,  $\text{Br}_2$ ; iii,  $\text{AgO}_2\text{CCF}_3$  or  $\text{Ag}_2\text{O}$ .



Scheme 2

shown in Scheme 1.<sup>5</sup> We have now established conditions under which the bromides (3) ( $n = 3-5$ ) react with tributyltin hydride to afford the parent peroxides (2)<sup>†</sup> (Scheme 2). An attractive feature of the method is that the required tributyltin hydride is generated *in situ* simply by mixing bis(tributyltin) oxide and polymethylhydrogen siloxane [equation (1)<sup>8</sup>].



Thus *cis*-9-bromo-7,8-dioxabicyclo[4.2.1]nonane (3b) (10 mmol) in benzene (5  $\text{cm}^3$ ) was added during 5 min to a stirred mixture of  $(\text{Bu}_3\text{Sn})_2\text{O}$  (7.5 mmol) and  $(\text{MeSiHO})_x$

<sup>†</sup> A preliminary attempt with 8-bromo-6,7-dioxabicyclo[3.2.1]octane (3a) was unsuccessful.<sup>5</sup>

(0.9 g) in benzene (15  $\text{cm}^3$ ) under nitrogen, followed by a few crystals of di-*t*-butyl hyponitrite. The mixture was stirred for *ca.* 18 h and the solvent then removed at 12 mmHg. The residue was partitioned between acetonitrile and hexane,<sup>9</sup> and evaporation of the acetonitrile layer afforded a mixture of (2b) and (3b) (plus a little  $\text{Bu}_3\text{Sn}$  compound), from which (2b) (50%) was isolated by low-temperature column chromatography ( $-20^\circ\text{C}$ ;  $\text{SiO}_2$ ;  $\text{CH}_2\text{Cl}_2$ ). The product was identified by comparison with literature data<sup>4</sup> and was further characterised by  $^{13}\text{C}$  n.m.r. spectroscopy,  $\delta$  78.02, 42.38, 33.85, and 23.13 p.p.m. The main advantage of this route to (2b) over that based on cyclohepta-1,3,5-triene<sup>4</sup> is that a difficult separation of sensitive isomeric endoperoxides is avoided.

A similar procedure starting with *cis*-10-bromo-8,9-dioxabicyclo[5.2.1]decane (3c) cleanly afforded (2c)<sup>3</sup> (50%) after 65 h. With *cis*-8-bromo-6,7-dioxabicyclo[3.2.1]decane (3a), however, extensive O-O cleavage accompanied and competed with reductive debromination and only 11% of (2a) could be isolated, even when the reaction time was cut to 1 h. Although the conversion of (3a) into (2a) is inefficient the reaction can be scaled up (*e.g.*  $\times 4$ ) without difficulty, and chromatographic purification of (2a) is easy. This, coupled with the fact that (3a) need not be rigorously purified (rapid removal of hydroperoxides by passage through a small quantity of  $\text{SiO}_2$  at  $-20^\circ\text{C}$  is adequate), and that the tributyltin hydride is generated *in situ*, render this a viable synthesis. 6,7-Dioxabicyclo[3.2.1]octane (2a) was obtained as white crystals, m.p.  $62-64^\circ\text{C}$ ;  $^1\text{H}$  n.m.r.  $\delta$  (200 MHz) 4.64 (2H, t,  $J$  5 Hz), 2.46 (1H, m), 2.40 (1H, A of AB,  $J$  11 Hz), 2.06 (2H, m), 1.80 (2H, m), and 1.54 (2H, m);  $^{13}\text{C}$  n.m.r.  $\delta$  76.42, 47.09, 30.75, and 17.95 p.p.m.; (Found:  $M^+$  114.0665;  $\text{C}_6\text{H}_{10}\text{O}_2$  requires  $M^+$  114.06808).

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