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

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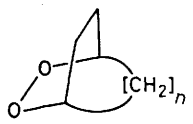
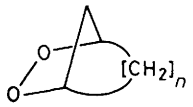
6,7-Dioxabicyclo[3.2.1]octane has been prepared from its *cis*-8-bromo derivative by reduction with tributyltin hydride generated *in situ* from bis(tributyltin) oxide and polymethylhydrogen siloxane; analogous reactions have afforded 7,8-dioxabicyclo[4.2.1]nonane and 8,9-dioxabicyclo[5.2.1]decane.

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.[1] 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.[2] In contrast no general route exists for the synthesis 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.[3] Adam[4] 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,[5] 2-bromo,[6] 2,4-dibromo,[3] and 1,5-dimethyl[7] 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.

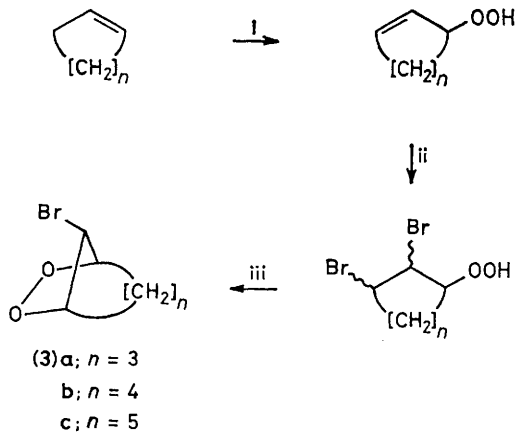


(1)

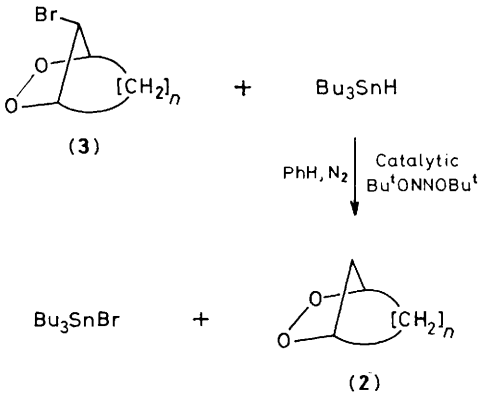


(2) **a**; *n* = 3
b; *n* = 4
c; *n* = 5

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, $^1O_2$; ii, Br_2; iii, AgO_2CCF_3 or Ag_2O.



Scheme 2

shown in Scheme 1.[5] We have now established conditions under which the bromides (**3**) (n = 3—5) react with tributyltin hydride to afford the parent peroxides (**2**)† (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)[8]].

$$x(Bu_3Sn)_2O + 2(MeSiHO)_x \rightarrow 2xBu_3SnH + 2(MeSiO_{1.5})_x \quad (1)$$

Thus *cis*-9-bromo-7,8-dioxabicyclo[4.2.1]nonane (**3b**) (10 mmol) in benzene (5 cm^3) was added during 5 min to a stirred mixture of $(Bu_3Sn)_2O$ (7.5 mmol) and $(MeSiHO)_x$ (0.9 g) in benzene (15 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,[9] and evaporation of the acetonitrile layer afforded a mixture of (**2b**) and (**3b**) (plus a little Bu_3Sn compound), from which (**2b**) (50%) was isolated by low-temperature column chromatography (−20 °C; SiO_2; CH_2Cl_2). The product was identified by comparison with literature data[4] and was further characterised by ^{13}C n.m.r. spectroscopy, δ 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[4] 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**)[3] (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.* × 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 SiO_2 at −20 °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 °C; ^1H n.m.r. δ (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}C n.m.r. δ 76.42, 47.09, 30.75, and 17.95 p.p.m.; (Found: M^+ 114.0665; $C_6H_{10}O_2$ requires M^+ 114.06808).

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

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