

A Flexible Route to [4.1.1]Propellanes

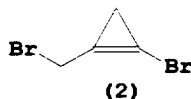
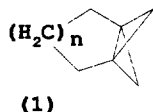
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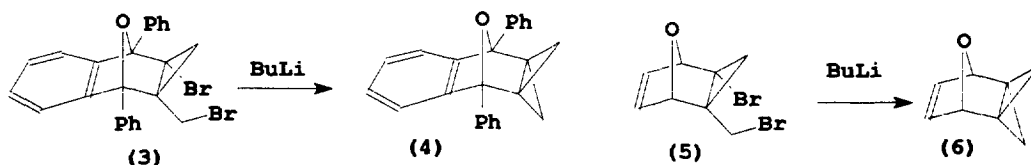
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Abstract: Reaction of Diels-Alder adducts of 1-bromo-2-bromomethylcyclopropene and either 1,3-dienes or furans with butyl lithium leads to a 1,3-dehalogenation to produce [4.1.1]propellanes. The oxygen bridged propellane derived from furan reacts with a second mol.equiv. of butyllithium by cleavage of the bridge with allylic rearrangement and the formation of a *cis*-3-butyl-[4.1.1]propell-4-en-2-ol. © 1997 Elsevier Science Ltd.

There has been considerable interest in the chemistry of highly strained propellanes.¹ The parent [2.1.1]- and [3.1.1]propellanes (1, *n* = 0,1) have been generated by dehalogenation of the corresponding 1,4-dihalobicyclo[2.1.1]hexane and 1,5-dihalobicyclo[3.1.1]heptane respectively,^{2,3} although the former compound is detectable in a nitrogen matrix at low temperature, and the latter can be detected even at somewhat higher temperatures, neither compound is long-lived at ambient temperature. The corresponding [4.1.1]propellane (1, *n* = 2) has been obtained by intramolecular addition of a carbene to an alkene and is stable enough to detect at ambient temperature.⁴ Although there are now many examples of related propellanes in which the methylene carbons of the bicyclobutane ring are bridged by a third ring, other examples of propellanes with these positions unsubstituted are relatively uncommon.¹ Related [4.1.1]- and [3.1.1]-propellanes having an additional bridge between the two methylene positions of the bicyclobutane ring have been prepared by trapping of transient 2,4-bridged bicyclo[1.1.0]but-1(3)-enes by [4+2]-cycloaddition to dienes such as diphenyl isobenzofuran⁵⁻⁷ or *N*-methyl-2,4-dimethylisindole.⁸ However, trapping of the parent bicyclo[1.1.0]but-1,3-ene was not successful.¹

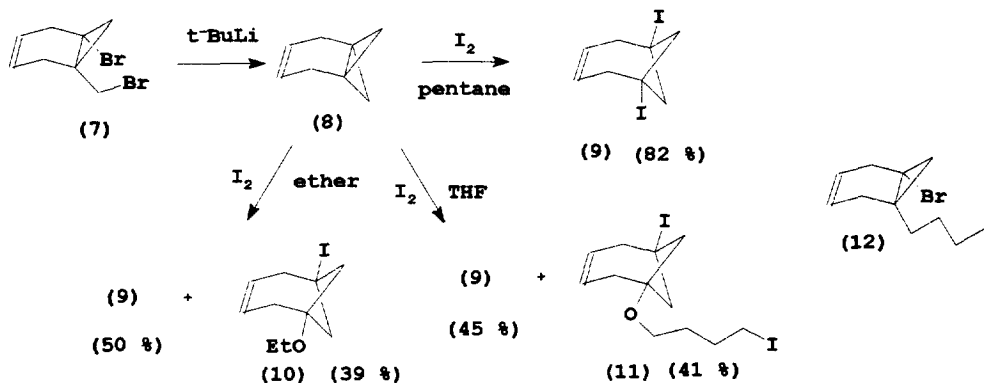
We reported some years ago that the reaction of 1,1-dibromo-2-bromomethylcyclopropanes with methyl lithium leads to a 1,3-debromination and the formation of a bicyclo[1.1.0]butane.⁹ This reaction has been widely used in the preparation of highly strained ring-systems, eg. in the work of Szeimies *et al.*¹ We recently reported that reaction of readily available 1,1,2-tribromo-2-bromomethylcyclopropane with methyl lithium leads to 1-bromo-2-bromomethylcyclopropene (2), which may be trapped in good yield by reaction with dienes, eg. as the adducts (3) and (5).¹⁰ We now find that, although these compounds appear to be unreactive towards methyl lithium, they did react with 1 mol.equiv. of *n*-butyllithium in hexane at -78 to 0 °C. Thus the adducts (3) and (5) were converted into the propellanes (4) (76 %) and (6) in good yield.¹¹





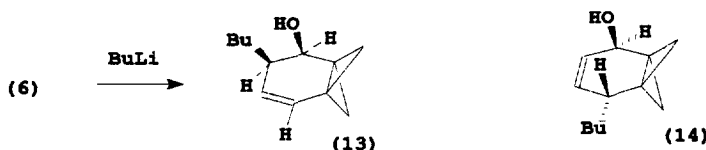
The ^1H n.m.r. spectrum of the propellane (6) included four discrete bicyclobutane hydrogens, two double doublets at δ 3.2 (J 7.7, 2.7 Hz) and 2.7 (J 7.7, 3.7 Hz) and two narrow doublets at 1.8 (J 3.7 Hz) and 1.6 (J 2.7 Hz). The signal at δ 3.2 is assigned to the bicyclobutane proton adjacent to the ether oxygen, and the coupling constant of 7.5 Hz is typical of a $^4J_{\text{H,H}}$ between the two exo-hydrogens of this ring system.¹²

In the same way, reaction of the butadiene adduct of (2), compound (7), with *t*-butyllithium in pentane-ether led to the parent [4.1.1]propell-3-ene (8) which could be purified by evaporation of the solvent at -5°C and 14 mmHg and then flash distillation at 1 mmHg.¹³ The hydrocarbon showed just four singlets in the ^1H n.m.r. spectrum, at 5.6 (2 H), 2.5 (4 H), 1.4 (2 H) and 1.0 (2 H). The lack of coupling between the bicyclobutane hydrogens in this case is surprising, but entirely in agreement with the corresponding hydrogens for [4.1.1]propellane.⁴ The hydrocarbon reacted with iodine in pentane to give the diiodide (9)^{1,15} but when the reaction was carried out in ether or tetrahydrofuran two products were obtained in each case, (9) and either (10)¹⁶ or (11).¹⁷

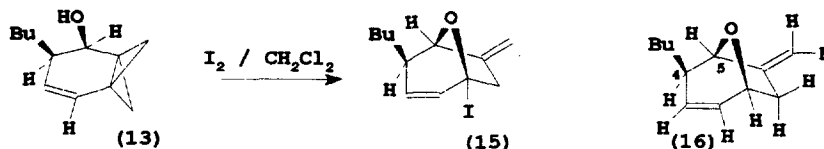


The formation of the ethers (10) and (11) may occur by solvation of an unstable bridged cation derived by addition of I^- to (8) followed by dealkylation of the derived oxonium ion by iodide ion. The formation of dimers and indeed of oligomers has been reported from radical addition to related systems such as [1.1.1]propellane,^{1,14} but no such products have yet been isolated in the present case.

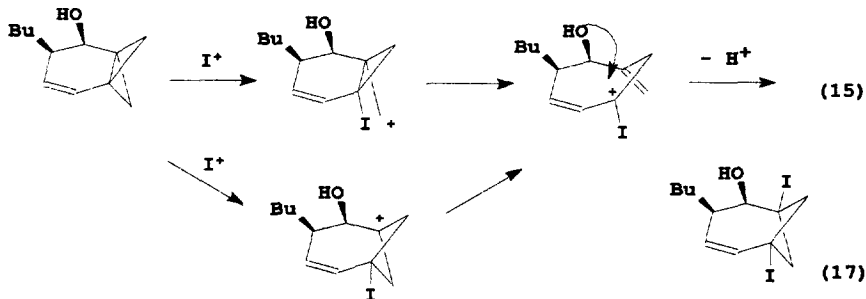
Although compound (4) was stable to reaction with a second mol.equiv. of butyllithium, compound (6) reacted rapidly under these conditions by opening of the furan ring without reaction at the bicyclobutane moiety. It was difficult to distinguish the product (13) absolutely by n.m.r.¹⁸ from structures such as (14) in which an alternative mode of furan opening had occurred, because coupling constants in the cyclohexenol were small.



However, compound (13) reacted with iodine in dichloromethane to give the ether (15)¹⁹ as the major product together with a minor amount of (16) (2.5:1).²⁰



Reduction of (15) with Li-Bu^tOH-THF at 20 °C gave (16) (84 %).²¹ The stereochemistry of the butyl group was assigned on the basis of the very small coupling constant between H-4 and the bridgehead proton H-5 in both compounds, typical of that for an exo-3-substituted compound.²² The formation of (15) may occur either through addition of iodonium ion to an external cyclopropane bond, though this would formally lead to a primary cyclopropylmethyl cation, or by similar addition to the bicyclobutane bridge bond, in either case followed by rearrangement. The addition of the HI generated in this reaction could then compete, leading to (16). However radical reactions have not yet been properly excluded.



In contrast, reaction of (13) with iodine in ether led to a 5:1 mixture of the iodoether (15) and diiodide (17).

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- It was difficult to obtain compound (6) pure due to its high volatility; however it was the only product by g.l.c. and reaction of (5) with 2 mol.equiv. gave (13), derived from (6) in 94 % yield.

12. Hoz, S. 'Bicyclo[1.1.0]butane' in *The Chemistry of the Cyclopropyl Group*, Ed. Z. Rappoport, Ch. 19, Vol. 2, 1121 - 1192, Wiley, 1987.
 13. The crude yield of (8) was estimated as 95 % by g.l.c., but the distilled yield free from solvent was 56 %, together with a further fraction containing solvent. Reaction of (7) with n-butyllithium also led to (8), but an additional compound was also obtained, provisionally characterised as the butylation product (12), and this became the major product when all (7) had been consumed (with 2.2 mol.equiv. of BuLi). Compound (8) showed δ_C 0.5, 22.3, 39.7, 121.9. It was essentially unchanged after 16 h at 20 °C in $CDCl_3$.
 14. Michl, J. 'Harnessing Strain: From [1.1.1]Propellanes to Tinkertoys', in *Strain and its Implications in Organic Chemistry*, NATO ASI Series, Vol. 273, Ed. de Meijere, A., 1989, 463 - 482.
 15. Compound (9) showed δ_C 126.0, 60.2, 49.3, 15.9; δ_H 5.22(2 H, t, J 1.6 Hz), 3.7 (2 H, complex d, J 10.6 Hz), 3.19 (2 H, complex d, J 10.6 Hz), 2.92 (4 H, br.s). The carbon signal at 60.2 was coupled to the hydrogen signals at 3.19 and 3.7, while that at 49.3 was coupled to the hydrogens at 2.9.
 16. Compound (10) showed δ_H 5.46 (1 H, sex.d, J 12.5 Hz), 5.19 (1 H, sex.d, J 12.5 Hz), 3.34 (2 H, q, J 7.0 Hz), 3.05 (2 H, complex, incl.d, J 9.9 Hz), 3.0 (2 H, br.s), 2.71 (2 H, complex, incl.d, J 9.9 Hz), 2.23 (2 H, br.s), 1.15 (3 H, t, J 7.0 Hz); δ_C 125.9d, 123.2d, 76.3s, 58.3t, 51.9t, 48.8t, 37.1t, 26.8s, 15.9q.
 17. Compound (11) showed δ_C 126.0, 123.0, 76.4, 61.8, 51.8, 48.7, 37.1, 31.1, 30.4, 26.5, 20.3, 6.7; δ_H 5.4 (1 H, dm, J 12.3 Hz), 5.2 (1 H, dm, J 12.3 Hz), 3.31 (2 H, t, J 6.2 Hz), 3.2 (2 H, t, J 6.9 Hz), 3.0 (4 H, m), 2.7 (2 H, complex d, J 9.9 Hz), 2.23 (2 H, br.s), 1.9 (2 H, m), 1.6 (2 H, m).
 18. The pmr spectrum of (13) included signals at 6.2 (1 H, ddd, J 9.2, 3.0, 0.8 Hz), 5.5 (1 H, dd, J 9.2, 2.3 Hz), 4.6 (1 H, ddd, J 6.6, 3.9, 0.8 Hz, reduced to br.d (J 3.9 Hz) on shaking with D_2O), 2.01 (1 H, dd, J 1.7, 6.8 Hz), 1.98 (1 H, m), 1.8 (1 H, dd, J 2.3, 6.8 Hz), 1.38 (1 H, d, J 6.6 Hz), 1.27 (1 H, dd, J 2.3, 1.0 Hz), 0.9 (3 H, br.t, J ca 7.1 Hz). Irradiation of the signal at δ 1.98 reduced those at 6.19, 5.5 and 4.6 to doublets or broad doublets. We thank the EPSRC NMR service in Edinburgh for obtaining these spectra at 600 MHz.
 19. Compound (15) showed 6.35 (1 H, dd, J 9.8, 1.5 Hz), 5.25 (1 H, ddd, J 9.8, 4.3, 2.0 Hz), 5.1 (1 H, narrow m), 5.0 (1 H, narrow m), 3.2 (1 H, d of narrow m, J 14.9 Hz), 3.1 (1 H, d of narrow m, J 14.9 Hz), 1.7 - 1.2 (8 H, complex), 0.9 (3 H, m); δ_C 150.4, 138.8, 128.0, 106.4, 82.8, 67.7, 56.0, 44.4, 32.8, 29.4, 22.7, 14.0.
 20. The ratio of (15) to (16) was rather variable, but some of the latter was formed even when the reaction was carried out in the presence of sodium carbonate.
 21. The p.m.r. spectrum of (16) was very similar to that for (15) except that one additional single-hydrogen signal appeared (at δ 4.49, dd, J 6.1, 4.3 Hz), and additional splittings appeared in the signal for one hydrogen of the methylene group (at δ 2.7, J 6.1) and in that for the lower field alkene signal (at δ 5.9, J 4.3 Hz).
 22. See eg., Klarner, F.-G., Schroer, D. *Chem.Ber.*, 1989, 122, 179.
- * Compound (8) also reacted with dimethyldisulphide in refluxing tetrahydrofuran over 48 h in the presence of AIBN to give a mixture from which 1,6-di(methylthio)bicyclo[4.1.1]oct-3-ene was isolated in 22 % yield.¹ Reaction of (8) with either tri-n-butyltin hydride or t-butyllithium in pentane led to complex products.¹