

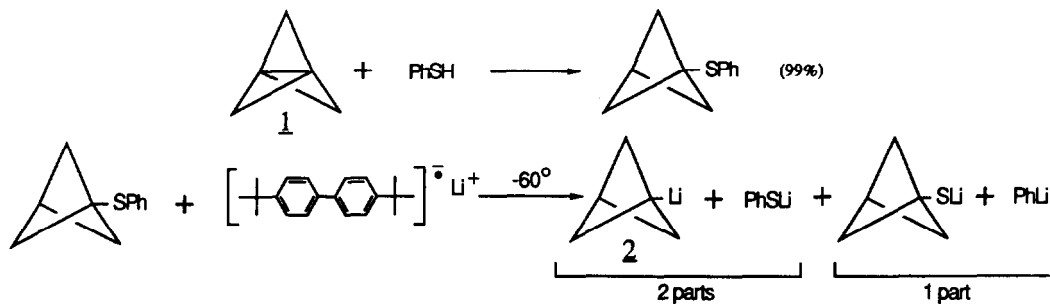
Formation and Reactions of 1-Lithiobicyclo[1.1.1]pentane

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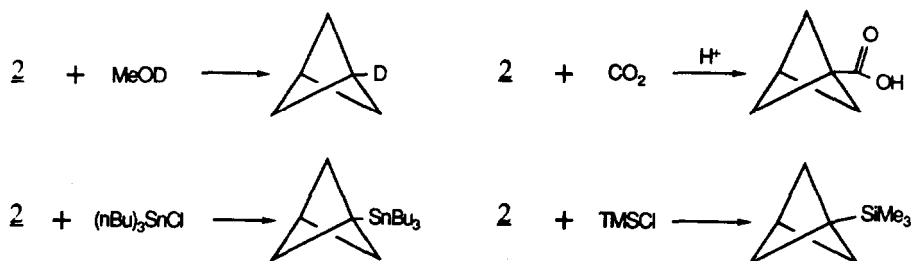
Summary: Bicyclopentyllithium was prepared in two steps from the readily available [1.1.1]propellane and proved to be a versatile intermediate in the preparation of a wide variety of 1-substituted bicyclopentanes.

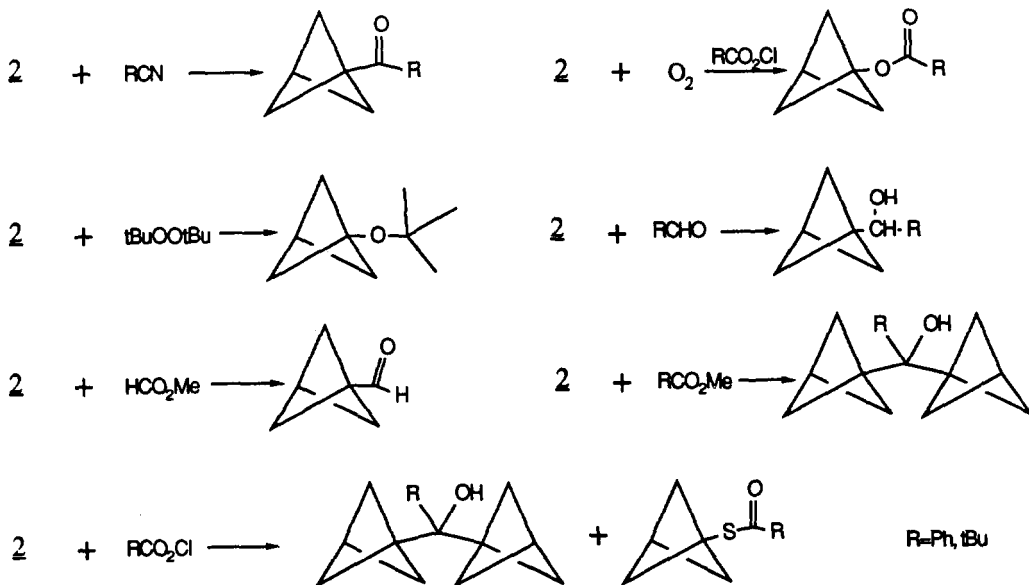
1-Substituted bicyclo[1.1.1]pentanes have been relatively difficult to prepare. The 1-chloro and 1-carboxylic ester were first prepared by free radical substitution on bicyclo[1.1.1]pentane,¹ which is itself difficult to prepare. Some compounds of this type have recently been obtained via free radical additions to [1.1.1]propellane (1),² which is now readily accessible via the simple synthesis developed by Szeimies.³ However, there are limitations to the types of groups which may be entered in this way.

We now report a simple route to 1-lithiobicyclo[1.1.1]pentane (2), and some reactions of this compound. The addition of thiophenol to 1 proceeds essentially quantitatively using equimolar quantities of the two reagents.³ An important advantage of this reaction over many of the free radical addition reactions is that the propellane does not need to be purified. The thiophenol is added to the crude reaction mixture (vacuum transferred away from excess alkylolithium) making the formation of bicyclo[1.1.1]pentyl phenyl sulfide a simple one pot procedure. The bridgehead sulfur may be reductively replaced by lithium via reaction with the lithium radical anion from 4,4'-bis-*t*-butylbiphenyl.⁴ The reaction is very slow at -78°C but proceeds readily at -60°C. The desired compound is the major product, but sulfur-phenyl bond cleavage also occurs to some extent:



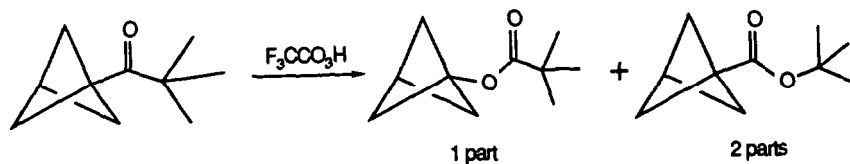
The lithio derivative reacts with the usual range of reagents, and some examples are⁵:



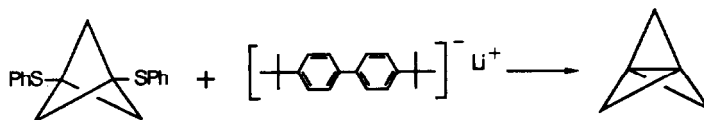


It was interesting to note that whereas methyl benzoate or methyl pivalate reacted to give tertiary alcohols, presumably via the intermediate ketone, the reaction of methyl formate gave only the aldehyde. This might result from the higher reactivity of methyl formate which can successfully compete with the ketone for **2**, or might result from the enhanced stability of the tetrahedral alkoxy intermediate (smaller substituents result in less steric crowding). The methine proton in bicyclo[1.1.1]pentyl tri-*n*-butyltin showed coupling to each of the three magnetic isotopes of tin: ^{119}Sn $J=179.45$ Hz, ^{117}Sn $J=171.04$ Hz, ^{115}Sn $J=156.06$ Hz. This unusually large bridgehead-bridgehead long range coupling is exhibited in other derivatives of bicyclo[1.1.1]pentane as well.⁶

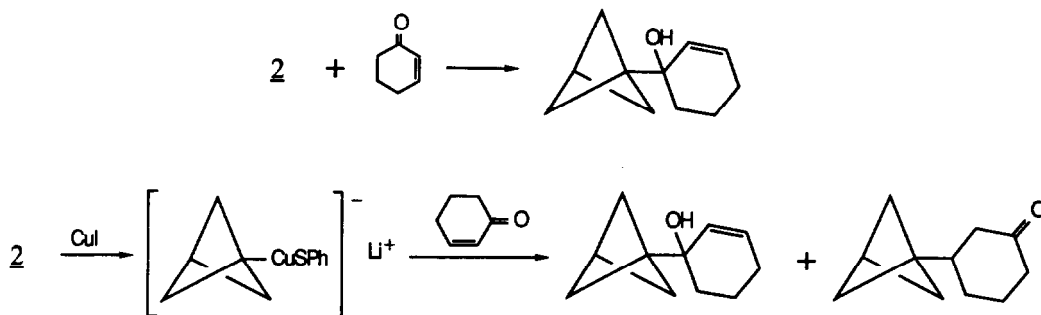
The reaction of bicyclo[1.1.1]pentyl *t*-butyl ketone with peroxytrifluoroacetic acid gave the two possible Baeyer-Villiger products in 1:2 ratio showing that the *t*-butyl group has twice the migratory aptitude of the bicyclopentyl group. This may be due to the increased electronegativity of the bridgehead carbon as compared to *t*-butyl, which results from the bond angle deformation.⁷



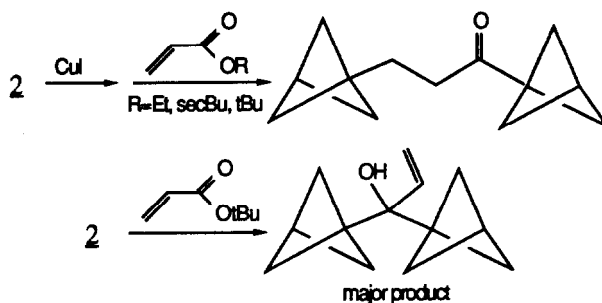
The addition of diphenyl disulfide to **1** gave the bis phenylthio adduct.² Its reaction with the radical anion simply regenerated **1** rather than giving the 1,3-bis anion.



Cuprate additions have proven useful for conjugate additions. Since phenylthiolate ion is present from the reaction which forms the anion, the addition of cuprous iodide probably forms a reagent of the type RCuSPh . Here we are fortunate, because phenylthiolate has been identified as the ligand of choice for preparing tertiary heterocuprates.⁸ Whereas the addition of **2** to cyclohexenone gave only 1,2-addition, the reaction in the presence of cuprous iodide gave a 1:1 mixture of 1,2 and 1,4-addition:



The reaction of the cuprate with ethyl, sec-butyl or tert-butyl acrylates gave 1,4-addition and replacement of the alkoxy group by bicyclopentyl. This may be contrasted with the reaction of **2** with t-butyl acrylate which gave mainly the bis 1,2-addition compounds, along with some of the 1,2 + 1,4 addition product:



The cuprate also reacted with octyl iodide to give 1-n-octylbicyclo[1.1.1]pentane.



In conclusion, this methodology provides a short, simple route for the large scale preparation of a wide variety of 1-substituted bicyclopentanes. Many of these compounds were previously virtually inaccessible and others could only be prepared using lengthy low yield syntheses. Bicyclopentane derivatives are unique because of the extremely short nonbonded distance between the bridgehead carbons (1.85 angstroms in the parent) and the large degree of through space orbital communication which results (of which large interbridgehead NMR coupling constants are but one manifestation.) The ready availability of derivatives of this ring system will hopefully pave the way to further insights into the behavior of strained molecules.

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References and Notes

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2. K. B. Wiberg, S. T. Waddell and K. E. Laidig, *Tetrahedron Lett.*, **27**, 1553 (1986). Since the publication of this paper we have successfully added a variety of ketones, esters, ethers, acetals, amines, silanes and phosphines across the central bond of the [1.1.1]propellane. Most of these reactions require that the propellane be purified, however.
3. K. Semmler, G. Szeimies and J. Belzner, *J. Am. Chem. Soc.*, **107**, 6410 (1985).
4. (a) C. G. Screttas and M. Micha-Screttas, *J. Org. Chem.*, **43**, 1064 (1978). (b) P. K. Freeman and L. L. Hutchinson, *Tetrahedron Lett.*, **22**, 1849 (1976).
5. The new compounds were readily identified by the characteristic proton NMR of the 1-substituted bicyclopentane skeleton. The methylene protons of the bicycle appear as a sharp singlet (or doublet of doublets if the 1-substituent is a chiral center) in the region δ 1.6- δ 2.3. The methine proton appears as a sharp singlet in the region δ 2.4- δ 2.9. Consistent mass spectra were obtained on all compounds.
6. In 1-deuterobicyclo[1.1.1]pentane the methine proton is split by 2.6 Hz, indicating that the two methine hydrogens of the parent compound split each other by approximately 18 Hz (see K. B. Wiberg and D. S. Connor, *J. Am. Chem. Soc.*, **88**, 4437 (1966)). In bicyclo[1.1.1]pentyl diphenylphosphine the methine proton is split by 29.61 Hz and in bicyclo[1.1.1]pentyl dimethyl phosphonate the methine proton is split by 55.92 Hz. These phosphorus containing derivatives of bicyclo[1.1.1]pentane were prepared via free radical addition reactions.
7. K. B. Wiberg, R. F. W. Bader and C. D. H. Lau, *J. Am. Chem. Soc.*, **109**, 1001 (1987).
8. G. H. Posner, C. E. Whitten and J. J. Sterling, *J. Am. Chem. Soc.*, **95**, 7788 (1973).

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