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# 9,9-Dimethyl-8,10-dioxapentacyclo[5.3.0.0$^{2,5}$.0$^{3,5}$.0$^{3,6}$]decane and naphthotetracyclo[5.1.0.0$^{1,6}$.0$^{2,7}$]oct-3-ene: new substituted [1.1.1]propellanes as precursors to 1,2,3,4-tetrafunctionalized bicyclo[1.1.1]pentanes

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**Abstract**—Two new substituted [1.1.1]propellanes have been generated from the corresponding bicyclo[1.1.0]butanes in either single-step (**1a**) or four-step procedures (**1b**). The observed degree of double lithiation of the bicyclo[1.1.0]butanes is discussed in the context of DFT computational results. Addition reactions across the central C(1)–C(3) bonds of the propellanes were studied. Only the propellane **1b** gave the biacetyl addition product.


## 1. Introduction

Polyfunctionalized bicyclo[1.1.1]pentanes (BCPs)[1] bearing functional substituents in addition to the two bridgehead ones are rare and sought-after as potential structural elements for molecular electronics and architecture.[2–4] Among a handful of such derivatives are 2,2-dichloro-[5] and polyfluoro derivatives,[6,7] which were obtained by direct halogenation of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid or its esters.[8] Further transformations of the halogens to other groups have not been successful. In contrast, transformations of the carboxyl groups proceeded smoothly,[7,9] which enable the generation of 2,2-dichloro[1.1.1]propellane.[9] Recently, chlorination of the 2,4-dimethylene derivative of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid and subsequent transformations of the halogenated products led to bicyclo[1.1.1]pentane-1,2,3,4-tetracarboxylic acid, the first example of tetrafunctionalized BCP **A**.[10]

A more versatile and general approach to polyfunctionalized BCPs **A** may, in principle, involve appropriately substituted [1.1.1]propellanes **B** (Fig. 1). Subsequent addition of biacetyl across the central bond of the propellane[11] introduces a carbonyl group amenable to further functional group manipulation.[12–14]

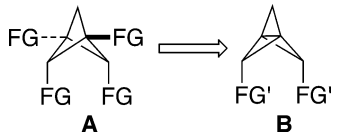
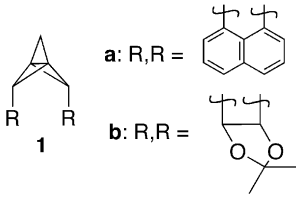



**Figure 1.** Retrosynthetic analysis for preparation of 1,2,3,4-tetrafunctionalized bicyclo[1.1.1]pentanes **A** through propellanes **B**.

Most [1.1.1]propellanes prepared to date are mono or geminally disubstituted derivatives of the parent [1.1.1]propellane or its 2,4-dimethylene or 2,4-trimethylene derivatives.[1,15] Only a handful of [1.1.1]propellanes are substituted with aryl,[16–18] vinyl[18] or alkoxymethyl[19,20] groups which are inert to propellane generation conditions and can be converted to the versatile carboxyl group. To our knowledge there is only one propellane with a benzyl group bridging the 2 and 4 positions,[16] which is a potential precursor to 1,2,3,4-tetrafuctionalized BCPs **A**. Unfortunately, the chemistry of this propellane has not been investigated.

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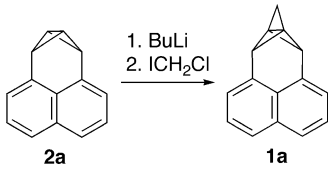
In order to develop synthetic access to tetrafunctionalized BCPs **A**, we focused on two new propellanes **1a** and **1b**. Here, we report the generation of the two substituted propellanes and some reactions at the central C–C bond with the emphases on the addition of biacetyl.

## 2. Results and discussion

### 2.1. Preparation of propellanes

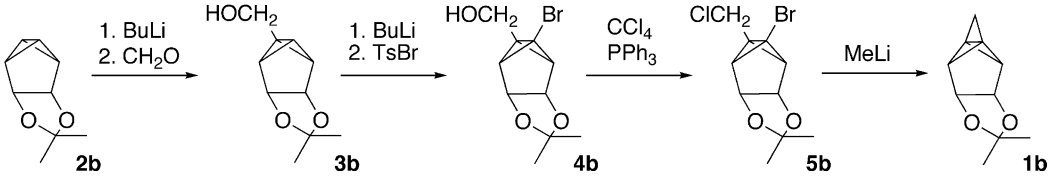
Propellanes **1a** and **1b** were prepared from appropriate bicyclo[1.1.0]butanes **2a** and **2b** using the methodology developed by Szeimies.[16] The former propellane was prepared in a single annelation step with $ClCH_2I$ taking advantage of the almost quantitative double deprotonation of **2a** (Scheme 1). The propellane **1a** was prepared in yields estimated at 30–40% and used as crude solutions in subsequent reactions.



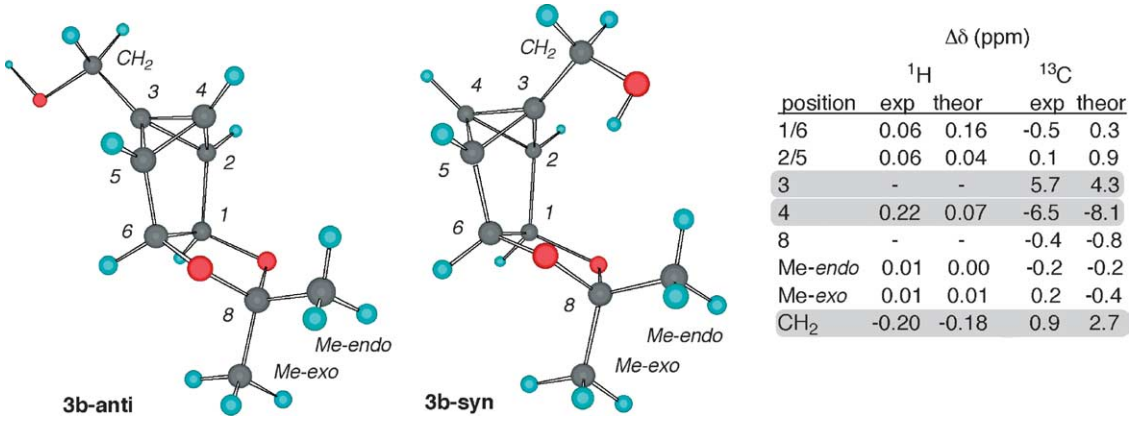

**Scheme 1.**

In contrast, propellane **1b** could not be prepared in the single-step procedure since the double deprotonation of **2b** was inefficient. Using *n*-BuLi, *sec*-BuLi or *tert*-BuLi at different temperatures, the double deprotonation occurred to less than 20%, as determined by quenching with $D_2O$ and GCMS analysis.[21] Also prolonged reaction times led to decomposition of the precursor **2b**. This necessitated the use of the four-step route[16] shown in Scheme 2. Thus, hydroxymethylation of **2b** gave alcohol **3b** as a mixture of two isomers in about 2:1 ratio contaminated with a more polar compound presumably the corresponding bis(hydroxymethyl) derivative. After purification on alumina, the isomeric mixture of alcohols **3b** was brominated and the resulting **4b** was subsequently converted to the dihalide **5b** using the general literature conditions.[16] To improve the separation of the pure **5b**, small amounts of EtOH were added in the end of the reaction to convert the residual $Ph_3P$ to the oxide. The overall average yield for the three steps was about 25%.

To assign stereochemistry of the two isomers formed during hydroxymethylation of **2b**, the minor isomer of **3b** was isolated chromatographically and the solid alcohol was purified by sublimation. NOESY experiments were inconclusive and the stereochemistry of the isomers was assigned based on a comparison of computational and experimental NMR data (Fig. 2). The analysis shows that the differences in theoretical chemical shifts $\Delta\delta$ (theor) for the *anti* and *syn* isomers follows the trend in the differences in experimental chemical shifts $\Delta\delta$ (exp) between the minor and major isomers. Perhaps the most diagnostic are the bridgehead positions of the bicyclo[1.1.0]butane ring and the hydroxymethyl group, which are most affected by the structural variation in the two isomers. Thus, the bridgehead carbon atom C(3) is significantly shielded, while C(4) is deshielded in the major and *syn* isomers relative to the minor and *anti*. Also, the $CH_2$ protons are significantly deshielded and the $^{13}C$ nucleus is shielded in the major and *syn* isomers relative to the minor and *anti*. This is consistent with general trends in exo/endo stereoisomers of bicycloalkanes.




**Scheme 2.**




Δδ (ppm)

| | $^1H$ | | $^{13}C$ | |
|---|---|---|---|---|
| position | exp | theor | exp | theor |
| 1/6 | 0.06 | 0.16 | -0.5 | 0.3 |
| 2/5 | 0.06 | 0.04 | 0.1 | 0.9 |
| 3 | - | - | 5.7 | 4.3 |
| 4 | 0.22 | 0.07 | -6.5 | -8.1 |
| 8 | - | - | -0.4 | -0.8 |
| Me-*endo* | 0.01 | 0.00 | -0.2 | -0.2 |
| Me-*exo* | 0.01 | 0.01 | 0.2 | -0.4 |
| $CH_2$ | -0.20 | -0.18 | 0.9 | 2.7 |

**Figure 2.** Optimized gas phase geometries for **3b**-anti and **3b**-syn isomers and comparison of the difference in experimental and computed NMR chemical shifts: $\Delta\delta$ (exp)=$\delta$ (**3b**-minor)−$\delta$ (**3b**-major); $\Delta\delta$ (theor)=$\delta$ (**3b**-anti)−$\delta$ (**3b**-syn). Theoretical results obtained at the B3LYP/6-31G(d,p) level of theory.