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An Improved Synthesis of Tetramethylcyclopentadiene

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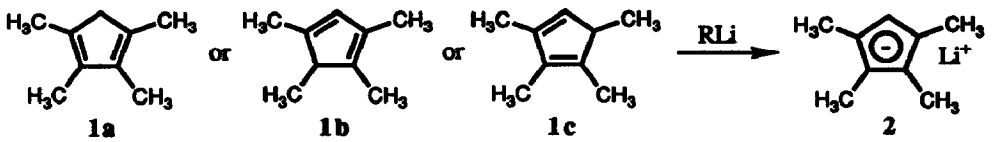
Abstract: A two-step synthesis of tetramethylcyclopentadiene, immediate precursor to substituted cyclopentadienyl ligands, has been developed based on a cyclodehydration reaction, providing this material rapidly and in relatively high yield.

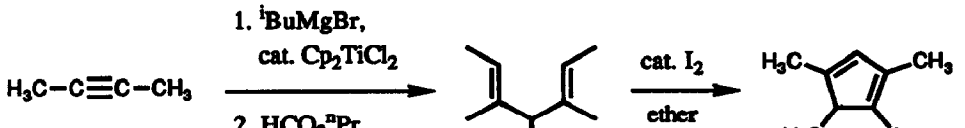
The tetramethylcyclopentadienyl ligand (2), prepared from tetramethylcyclopentadiene (1a-c), is finding increasing use in transition metal chemistry.[1] Like the more common pentamethycyclopentadienyl group, 2 tends to impart advantageous solubility and stability to many of its complexes. However, it is somewhat less electron donating and sterically demanding,[1a] which can have an advantageous influence on the reactivity of complexes. Further, tetramethylcyclopentadiene has the important advantage that it is easily alkylated at the remaining unsubstituted ring position, and this has been used to prepare functionalized tetramethylcyclopentadienes,[2] as well as bridging bis(tetramethylcyclopentadienyl) ligands.[3]



1a **1b** **1c** **2**

To date, tetramethylcyclopentadiene has been prepared by essentially a single method,[3a] involving the dehydration of a cyclopentenol, which in turn is prepared mainly by aldol chemistry. This is a three-step procedure which requires 2-3 days and provides 1 in approximately 21% overall yield. In the course of investigating the cyclodehydration of doubly allylic alcohols to cyclopentadienes, we had occasion to study such reactions of dienol 3. This cyclodehydration offered the possibility of a two-step synthesis of 1, and thus we explored the viability of this approach. A mechanistic study of this reaction in superacid has been reported,[4] and the corresponding tertiary alcohol is known to cyclize efficiently to provide pentamethylcyclopentadiene.[5]

The requisite alcohol precursor 3 is conveniently prepared from 2-butyne using the titanocene dichloride catalyzed hydromagnesiation developed by Sato.[6] Reaction of the intermediate E-2-butenyl Grignard with propyl formate gives the secondary alcohol in 65% yield as strictly the E,E isomer.[7] Although other geometric isomers of this alcohol are readily prepared,[8,9] the E,E isomer undergoes cyclodehydration to 1 more



3 **1b**

efficiently (see below). Alcohol 3, prepared by a multistep procedure, was a key intermediate in a total synthesis of verrucosidin.[10]

Cyclodehydration of 3 is best accomplished by treatment with catalytic amount of iodine in ether solvent. Slow addition of the alcohol to the dehydration catalyst tends to minimize the formation of dimeric (and probably polymeric) byproducts. The tetramethylcyclopentadiene is isolated by trap-to-trap distillation (purity ~ 90%) and appears to be a single isomer (**1b**) by ^{1}H NMR.[11] Based on isolated yields, we observe that the E,E-alcohol 3 undergoes cyclodehydration more efficiently (56%, starting with 5g of 3) than does a Z,Z/Z,E mixture[9] of isomeric alcohols (< 40%), which has also been reported in a mechanistic study of these reactions in superacid media.[4] Thus, the two-step preparation of tetramethylcyclopentadiene from 2-butyne proceeds in 36% overall yield and can be completed in a single day.

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7. The ^{1}H NMR spectrum of 3 in $CDCl_3$ agreed closely with that previously reported[4] in CCl_4 solvent.
8. a. A less direct approach to 3 based on a report[8b] of syn addition of HI to alkynes was briefly explored, but this was found to give strictly Z-2-butenyl iodide, the product of anti addition. b. Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, 675-676.
9. We have found that conversion of commercially available 2-bromo-2-butene (Z:E ~90:10) to the corresponding vinyllithium[5] followed by reaction with propyl formate yields a mixture of alcohols isomeric to 3 as a 70:30 mixture of ZZ and ZE isomers in 80% yield.
10. Hatakeyama, S.; Sakurai, K.; Numata, H.; Ochi, N.; Takano, S. *J. Am. Chem. Soc.* **1988**, *110*, 5201-5203.
11. Interestingly, although the previous syntheses report this diene exclusively as the C_2 isomer **1a**,[1,3a,c] our synthesis affords strictly **1b**, which is consistent with the mechanism of formation.[4] ^{1}H NMR ($CDCl_3$) closely matches that reported previously (CCl_4 solvent): Kiselev, V. d.; Sakhabutdinov, A. G.; Shakirov, I. M.; Konovalov, A. I. *Zh. Org. Khim.* **1991**, *27*, 1641-1648. It has been reported that **1a** is more stable than the other isomers, but that equilibration does not occur at room temperature: Mironov, V. A.; Sobolev, E. V.; Elizarova, A. N. *Tetrahedron* **1963**, *19*, 1939-58.

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