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A USEFUL APPROACH TO TRICYCLIC COMPOUNDS AND MEDIUM RING DIKETONES THROUGH THE PHOSPHONIOSILYLATION REACTION.

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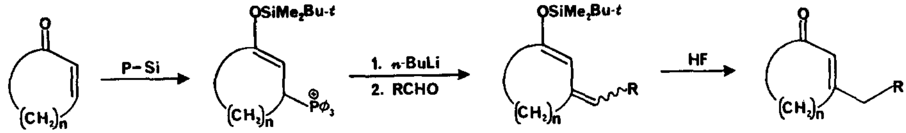
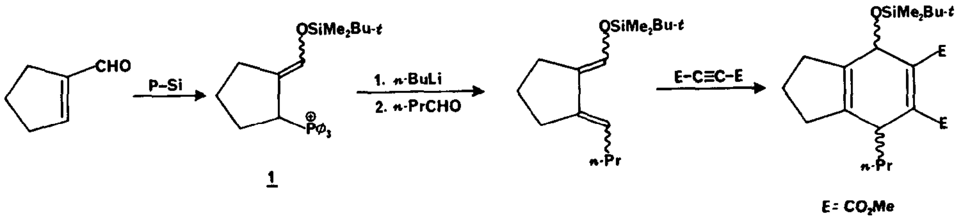
Summary: The use of the "P-Si" reaction in the construction of tricyclic structures has been probed. One example of the preparation of a medium ring compound is also provided.

We have discovered recently that a variety of enones and enals can be readily phosphoniosilylated through the use of triphenylphosphine in combination with t-butyldimethylsilyl triflate.[1] The resulting phosphonium enol silyl ethers provide access in turn through Wittig chemistry to dienol silyl ethers, useful intermediates in the preparation of β-functionalized enones. We have also found that cyclopentene-1-carboxaldehyde can be carried through this phosphoniosilylation ("P-Si")-Wittig sequence to yield a novel 1,2-dialkylidenecyclopentane derivative, a compound of some considerable use in the preparation of substituted hydrindanes by subsequent Diels-Alder chemistry.



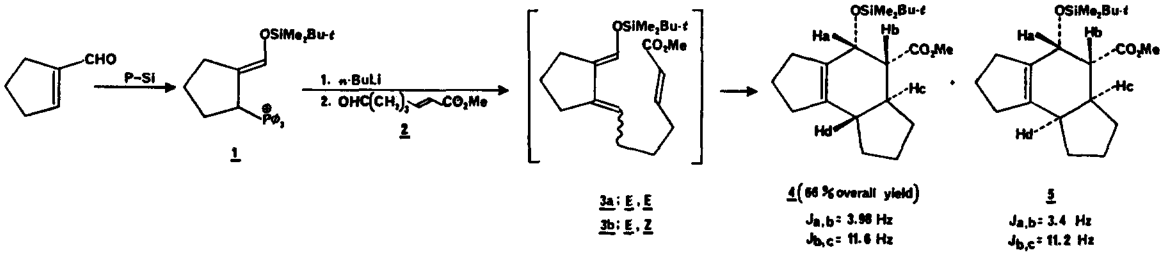
(a)



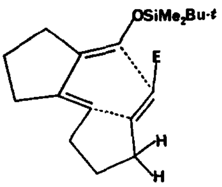
(b)

In reviewing the nature of the transformations that can be brought about by this chemistry, we realized that the "P-Si" reaction might be combined in a very favorable way with the intramolecular Diels-Alder reaction to give access to tricyclic structures containing a carbon-carbon double bond at a ring fusion site.[2] Accordingly such intermediates could further be used to access medium ring structures through subsequent ozonolysis.

To test these notions the "P-Si" product of cyclopentene-1-carboxaldehyde was combined in a Wittig reaction with methyl 7-oxohept-2-enoate.[3]

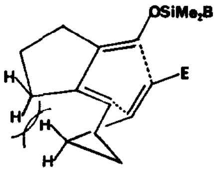


Interestingly, under the conditions of the Wittig reaction, the intramolecular Diels-Alder reaction ensued in part to produce some of the desired tricyclic compound **4**. The cycloaddition step was completed by heating the crude reaction products in benzene at 50 °C for 3 h. From an analysis of the ^{1}H NMR coupling constants we were able to make an assignment of stereochemistry to the major cycloadduct as depicted in structure **4**, an assignment which in turn leads us to assign E,E-stereochemistry to the starting diene system. The coupling constants observed for **4** are related closely to those reported for similar systems prepared by Diels-Alder chemistry.[4] Our NMR based structure assignment was further corroborated by an X-ray analysis on the structurally related 6,6,6-system (vide infra). The Diels-Alder reaction thus takes place via an endo transition state **A** rather than the sterically more encumbered exo transition state **B** which would place the bridge linking diene and dienophile into severe steric confrontation with the five-membered ring.[5]



A

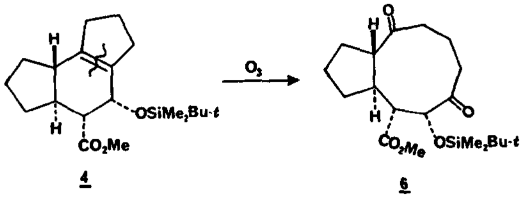
versus

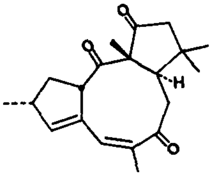


B

A small amount of product (< 4%) was also isolated which by ^{1}H NMR analysis was assigned structure **5**. This compound presumably comes from the E,Z-diene **3b** via an endo transition state. Some of the unreacted diene **3b** (~6%) was also present.

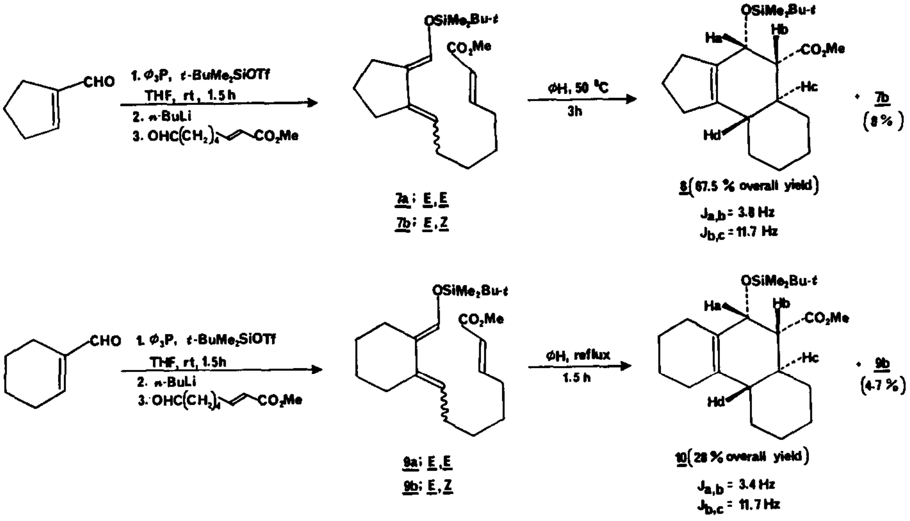
Compound **4** was subjected to ozonolysis in order to determine whether it could serve as a precursor to a nine-membered ring. Indeed, this reaction proceeded in 85% yield to provide the crystalline diketone **6**. A single crystal X-ray analysis revealed that the ozonolysis reaction had proceeded without epimerization of the centers of asymmetry. Intermediate **6** bears some resemblance to the nine-membered ring containing diterpene jatrophatrione,[6] a compound which has been of some synthetic interest to our group and which might well be procurable by such an intramolecular Diels-Alder/ozonolysis strategy.





Jatrophatrione

In order to further test the "P-Si", intramolecular Diels-Alder methodology, the 5,6,6 and 6,6,6 systems were also synthesized as shown in the accompanying schemes. An X-ray structure analysis was carried out on **10** which further confirmed the ^{1}H NMR based assignments. Additionally, a small portion of the unreacted E,Z-diene was isolated in each case.



Because of its overall simplicity, we believe that the present methodology may prove valuable in the construction of natural products possessing multiply fused ring systems.[7] Additionally, access to functionalized medium ring structures is possible, a feature which will be explored further.[8]

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