Pyrrolidine-Catalyzed Reactions between α,β-Unsaturated Carbonyl Compounds and Cyclopentadiene: A Convenient Approach to 1,2- and 1,5-Dihydropentalenes

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Received May 30, 1989

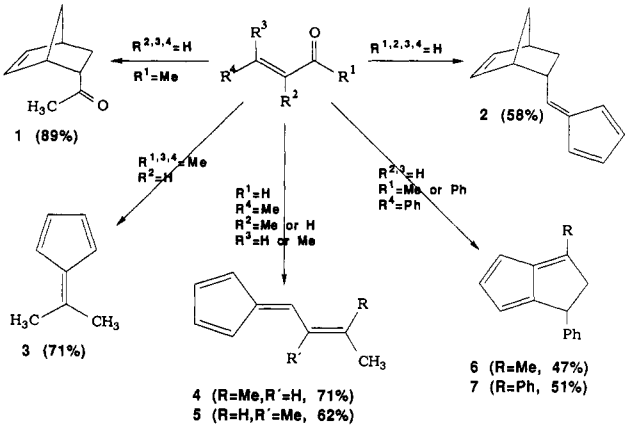
Summary: The reaction between cyclopentadiene and α,β-unsaturated carbonyl compounds in the presence of pyrrolidine gives rise to five different reaction pathways depending on the structure of the starting materials. For phenyl-substituted enones a high-yield one-pot synthesis of 1,2-dihydropentalenes is described.

Sir: The synthesis of 6-substituted pentafulvenes via pyrrolidine-catalyzed condensation between cyclopentadiene and ketones or aldehydes was developed by Stone and Little.[1] Corresponding reactions with α,β-unsaturated carbonyl compounds seem not to have been investigated however. The classical Thiele procedure,[2] using NaOEt in ethanol as base, gives only poor results concerning the formation of substituted vinylpentafulvenes.[3] For the synthesis of alkyl- and aryl-substitued 1,2-dihydropentalenes we needed vinylpentafluvenes in high yield since the latter have been demonstrated to be excellent starting materials for intramolecular electrocyclizations.[4] Therefore, we examined the reactions of a series of α,β-unsaturated carbonyl compounds with cyclopentadiene in the presence of pyrrolidine[5] in the hope of generating directly vinylpentafulvenes or dihydropentalenes.

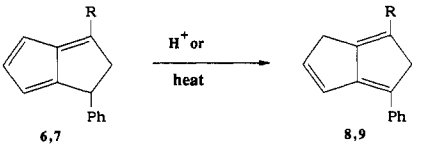
Scheme I gives a summary of the results: 3-butenone (entry a) gave exclusively the Diels–Alder product 1 even after prolonged reaction time (12 h instead of the normal 30 min). This coincides with the results Little[1] found when trying to generate pentafulvenes from sterically hindered ketones. In case (a) the [4 + 2] cycloaddition was by far the fastest reaction step and no secondary addition by the cyclopentadienyl anion (or the pyrrolidine to form the immonium intermediate) was possible. Using acrolein (entry b) as Michael substrate, the [4 + 2] cycloaddition again was the first step; consequently, in this case pentafulvene formation took place in a subsequent step. The complex pentafulvene **2**[6] was formed in moderate yield (58%) in this one-pot reaction; starting directly with the easily prepared norbornenealdehyde,[7] **2** is formed in about 72% yield.

In the above examples, the pentafulvene-forming step was slower than the cycloaddition reaction, a situation which changes when the enone carries electron-donating substituents. Product **3**, which could be isolated from reaction with mesityl oxide[8] (entry c) arose via Michael addition and subsequent retro-Aldol type reaction. The low reactivity of the carbonyl group could be enhanced by employing senecialdehyde (entry d). In this case and also in the tiglic aldehyde (entry d) the vinylpentafulvenes **4** and **5** were formed without competing Michael reaction or [4 + 2] cycloaddition. For the phenyl-substituted enones benzalacetone (entry e) and benzalacetophenone (entry e) conversion to the desired 1,2-dihydropentalenes took place in situ. The intermediacy of a Michael type adduct is reasonable; however, the only isolable comounds were the 1,2- and 1,5-dihydropentalenes. The 1,2-isomers **6**[9] and **7**[10] were converted to their 1,5-isomers **8**[11] and **9**[10] by acid catalysis or simply on prolonged heating (Scheme II). Therefore, the yield for the 1,2-isomer dropped significantly when large-scale (1–2 mol[12]) instead of the normal 0.1-mol reactions[5] were performed. On the other hand, this isomerization could be utilized for a high-yield synthesis of 1,5-dihydropentalenes. These compounds could represent versatile intermediates in the synthesis of complex polyquinane structures.

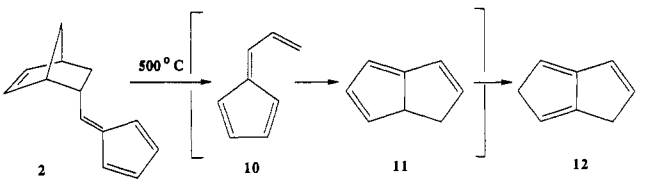
Scheme I. Reactions of Cyclopentadiene with Unsaturated Carbonyl Compounds in the Presence of Pyrrolidine



Scheme II. Conversion of 1,2-Dihydropentalenes into 1,5-Dihydropentalenes



Scheme III. Flash Vacuum Thermolysis of Pentafulvene 2



(1) Stone, K. J.; Little, R. D. *J. Org. Chem.* **1984**, *49*, 1849.
(2) Thiele, J.; Balhorn, H. *Justus Liebigs Ann. Chem.* **1906**, *348*, 1.
(3) Neuenschwander, M.; Meuche, D.; Schaltegger, H. *Helv. Chim. Acta* **1963**, *46*, 1760. Neuenschwander, M.; Meuche, D.; Schaltegger, H. *Helv. Chim. Acta* **1964**, *47*, 1022.
(4) Gajewski, J. J.; Cavender, C. J. *Tetrahedron Lett.* **1971**, 1057.
(5) Standard procedure: 0.2 mol of pyrrolidine was added (15 min) to a solution of 0.1 mol of enone and 0.3 mol of cyclopentadiene (freshly prepared[17]) in 90 mL of methanol at room temperature. After stirring for 30 min at room temperature the mixture was treated with 0.21 mol of acetic acid and extracted with 2 × 200 mL ether. The ether layer was washed with 2 × 100 mL water and 150 mL of brine. All products were distilled at reduced pressure without decomposition.
(6) Orange, oil, bp 68–72 °C (0.05 Torr), endo:exo ratio = 92:8.
(7) Diels, O.; Alder, K. *Justus Liebigs Ann. Chem.* **1928**, *460*, 98.
(8) Saegusa, T.; Ito, Y.; Tomita, S. *J. Am.* Chem. *Soc.* **1971**, *93*, 5656.
(9) Red oil, bp 116–118 °C (0.1 Torr).
(10) These compounds have been isolatd as side products (4%) using benzalacetophenone in the classical Thiele procedure:[2] Cioranescu, E.; Bucur, A.; Mihai, G.; Mateescu, G.; Nenitzescu, C. D. *Chem. Ber.* **1962**, *95*, 2325.
(11) Orange crystals, mp 64–66 °C.
(12) The yield of the 1,2-dihydropentalene **6** (up to 71%) could be increased by distillation of the compound at 10^{-4} Torr.

0022-3263/89/1954-4981$01.50/0

In principle, these compounds could be also prepared by the well known Hafner route[13] by using the corresponding 8-(dialkylamino)-substituted 6-vinylpentafulvenes. Whereas this reaction sequence is a three-step procedure (pentafulvene formation, cyclization, and exchange of the dialkylamino substituent), the way described here is a high-yield one-step reaction.

The product types from entries b, d, and e constitute valuable precursors which can be transformed into interesting compounds. Thus, the vinylpentafulvenes **4** and **5** were isomerized to the corresponding 1,5-dihydropentalenes by flash thermolysis. Most effective for this purpose was the flash vacuum thermolysis of the "cyclopentadiene protected" parent vinylpentafulvene **2**. At temperatures between 450 °C and 520 °C[14] cycloadduct **2** loses cyclopentadiene and gives the vinylpentafulvene **10**, which spontaneously cyclizes to the 1,6a-dihydropentalene **11** (Scheme III). This intermediacy product could not be isolated but immediately rearranges to the 1,5-dihydropentalene **12**[15] via 1,5-hydrogen migrations. Although this cyclization–rearrangement sequence was originally reported by Gajewski and Cavender,[4] it was not exploited for synthesis until now (only 10 mg of **12** could be made by direct vinylpentafulvene static thermolysis until now[4]). In our case, **12** could be isolated in 2–3-g quantities by thermolysis of 6 g of **2** in about 30 min. This synthetic methodology competes very well with the cyclooctatetraene thermolysis route developed by Meier and co-workers.[16] Furthermore, it should be easily applied to acceptor-substituted acroleins as starting materials. Investigations using this concept are in progress.

Acknowledgment. I thank the Fonds der Chemischen Industrie (Liebig-Stipendium) and the Universitätsbund Würzburg for financial support.

Supplementary Material Available: Spectral data for pyrrolidine-catalyzed reactions between α,β-unsaturated carbonyl compounds and cyclopentadiene (3 pages). Ordering information is given on any current masthead page.

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(14) 30-cm quartz thermolysis tube, 0.02 Torr of pressure.
(15) Katz, T. J.; Rosenberger, M.; O'Hara, R. K. *J. Am. Chem. Soc.* **1964**, *86*, 249.
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A Convergent Synthesis of Polyol Chains

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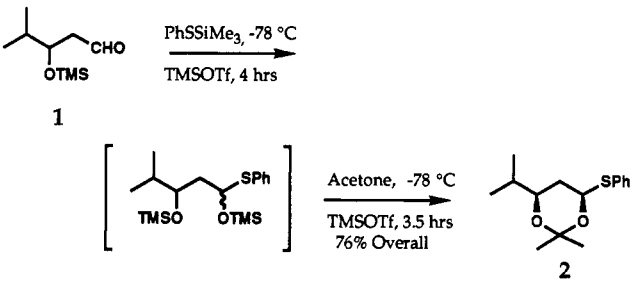
Received August 4, 1989

Summary: A new method is described for the convergent synthesis of polyol chains in which two chains are coupled with control of the newly formed stereogenic center.

Sir: Advances in asymmetric synthesis[1] over the last decade have made the construction of many simple polyol chains routine, but larger chains still represent a formidable challenge. A method is described herein which allows polyol chains to be coupled with control of the newly formed stereogenic center. This is a problem for which very few general solutions have been reported.[2,3] Our new method will dramatically simplify the synthesis of large polyol chains because it allows them to be prepared from readily available smaller chains by a *convergent* strategy.

This method is designed around new 1,3-diol synthons: 6-alkyl-4-(phenylthio)-1,3-dioxanes (e.g. **2**). These synthons are protected β-hydroxy aldehydes and can be prepared from either β-hydroxy esters[4,5] or homoallylic alcohols.[6,7] The 1,3-diol synthon **2** was prepared as a single isomer[8] by treating 4-methyl-3-[(trimethylsilyl)oxy]pentanal (**1**) (prepared in two steps from the homoallylic alcohol 2-methyl-5-hexen-3-ol) with (phenylthio)trimethylsilane and catalytic trimethylsilyl triflate to give a mixture of hemithioacetals,[9] followed by treatment with acetone and catalytic trimethylsilyl triflate.[10] This sequence can



be performed in one pot but is more reliable when the intermediate hemithioacetals are isolated. The product slowly decomposes under the reaction conditions, so the

(1) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, New York, 1985; Vol. 1–5.
(2) For a recent approach, see: Mori, Y.; Kuhara, M.; Takeuchi, A.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5419–5422. Mori, Y.; Takeuchi, A.; Kageyama, H.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5419–5422.
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(8) All new compounds were characterized by ^1H and ^{13}C NMR, IR, and C, H analyses or HRMS. Preparation of compounds **2** and **5**, as well as spectral data for compounds **2**, **5**, and **9** are given in the supplementary material.
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(10) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, 1357–1358.

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