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Tandem Use of Reductive and Radical Cyclization Protocols in an Approach to the First σ-Allyl Cation

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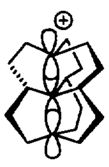
Abstract: The reduction of **8** with magnesium, chlorotrimethylsilane, and iodine to give **9** and the cyclization of **12** to **14** in the presence of tris(trimethylsilyl)silane and AIBN provide a convenient route to a triquinane carrying a two-carbon chain in each ring segment.

Keywords: *cyclization, polyquinanes, reduction, ring transformations, sulfur compounds*

A review of homoaromaticity authored by Paquette in 1978 [1] described the combination of colinear atomic pπ orbitals as in **1**. In particular, this arrangement was noted to be cylindrically symmetrical about the bond axis, to lack angular momentum, and to be nondegenerate. The commonly prevailing π contributions to p orbital interactions are seen to be completely factored out, such that examination of pure pp-σ interaction is made possible. Similar considerations apply to the so-called σ-allyl cation arrangement **2**. Carbocation **3** eventually came to be regarded from the theoretical vantage point as a possible prototype of such enforced alignment [2]. However, Lipkowitz did not find it possible at that time to distinguish definitively whether the ground state of this cation would be the alluring nonclassical species **3** [3] or consist of the rapidly equilibrating isomer pair **4** ⇄ **4'**. A more

1

2



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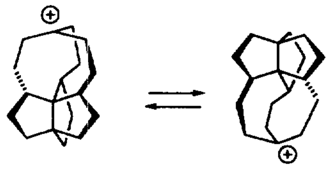
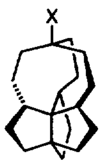


4 **4'**



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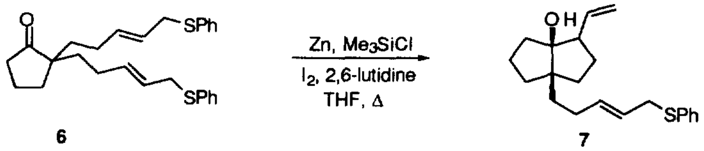
recent analysis of this problem at the hybrid HF-DFT level by Baldridge, *et al* [4] comes down in favor of the double well minimum potential model defined by the equilibrating classical cation pair.

Under these circumstances, it would clearly be of interest to prepare the functionalized capped propellane **5** in enantioenriched condition. With loss of X^-, the incipient cationic carbon could move along the propellane axis toward the central carbon atom and set the stage for the direct evolution of σ-allyl character. Since **3** is achiral, each ionizing event would result directly in racemization. Alternatively, should the symmetric combination of end-on p orbitals not develop, ionization to chiral **4** would not be accompanied with net racemization as long as the barrier to its interconversion with **4'** was not exceeded. In this connection, we recognize that should the barrier to racemization be as low as predicted by Baldridge (*ca* 14 kcal/mol) [4], the ^{1}H and ^{13}C NMR spectra of this alluring cation should manifest C_3 rather than C_{3h} symmetry below 0 °C.

A possible way to synthesize the relatively rigid superstructure resident in **3** has been described in the preceding paper [5]. This plan is designed to utilize a stereochemically defined trivinyl [3.3.3]propellane as the advanced intermediate that will ultimately give rise to **3**. Herein we describe an expedient route to a fused triquinane system holding the potential for conversion to this hydrocarbon. A noteworthy feature of the synthetic protocol is the sequential manner in which reductive and radical ring closures are deployed.

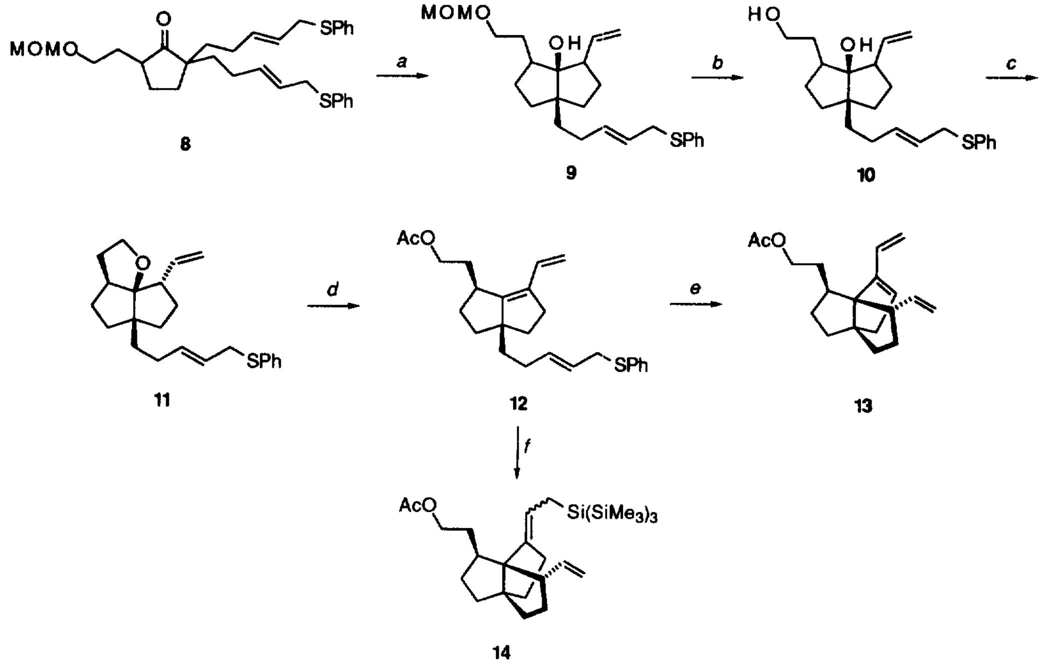
The following initial experiment served to illustrate lines of application for the reductive maneuver. Reaction of **6** [5] with zinc, chlorotrimethylsilane, iodine, and 2,6-lutidine in refluxing THF [6] for 24 h gave bicyclic alcohol **7** in 43% yield along with 28% of unconsumed ketone. The relative ease with which cyclization materialized in this example prompted its application to the more highly substituted congener **8**.



Quite unexpectedly, ketone **8** gave rise to a complex reaction mixture when comparably treated. This complication prompted us to examine the modification developed by Hutchinson which involves exposure to magnesium, chlorotrimethylsilane, and iodine in THF *at room temperature* [7]. As seen in Scheme 1, conversion to diquinane **9** was now realized in 37% yield. The two stereoisomers that were formed were not separated.

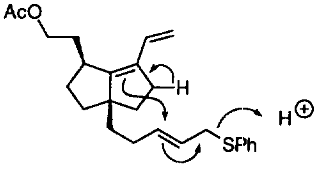
A two-step sequence involving hydrolytic removal of the MOM protecting group and cyclization of the diol in the presence of *N,N'*-thiocarbonyldiimidazole, Hunig's base, and DMAP [8], with ensuing chromatography on silica gel allowed for isolation of isomerically pure **11** [5].

Scheme 1



[a] Mg, Me_3SiCl, I_2, THF, rt, 113 h (37%). [b] HCl, MeOH, THF, rt, 42 h (73%). [c] $Im_2C{=}S$, $(i\text{-}Pr)_2NEt$, DMAP, CH_2Cl_2, rt, 50 h; chromatography on SiO_2 (25% of isomer shown). [d] *p*-TsOAc, CH_3CN, rt, 3 h (62%). [e] *p*-TsOAc, CH_3CN, reflux, 71 h (84%). [f] $(Me_3)_3SiH$, AIBN, toluene, 80 °C, 12 h (51%).

The structural features of **11** led us to predict that electrophile-induced ring opening of its tetrahydrofuran ring would proceed regioselectively with loss of the allylic proton. In fact, the anticipated conversion to **12** does occur at room temperature in acetonitrile containing 5 equiv of acetyl *p*-toluenesulfonate [9]. As experience was gained with this reaction, we came to recognize that the **11** → **12** transformation is time- and temperature-dependent. At the reflux temperature of acetonitrile, both intermediates are converted into the triquinane triene **13**. Although the mechanistic details of this process have not been investigated, we envision the acid-catalyzed elimination of thiophenol as depicted in **A** to be a reasonable possibility.



A

In view of the apparent ease associated with closure of the third five-membered ring, attention was now directed toward accomplishing the same objective by a novel radical process. Indeed, exposure of **12** to tris(trimethylsilyl)silane and AIBN in refluxing toluene [10] generated **14** in an unoptimized 51% yield. NOE studies provided confirmation of the relative orientation of the β-acetoxyethyl and vinyl side chains. The third substituent is an allylsilane, which can in principle be converted into a properly stereodirected vinyl group by protonation under thermodynamic conditions.

Our assumption that 5-phenylthio-3-pentenyl fragments such as those residing in **6** and **8** could be usefully deployed under reductive and radical conditions has been shown to be workable. A cationic variant was also found to proceed satisfactorily. We anticipate that these findings will provide the proper impetus for gaining access to the capped triquinane **5** [11].

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References and Notes

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[11] All new compounds described herein exhibited IR, ^{1}H NMR, ^{13}C NMR, and MS spectral data in satisfactory agreement with the assigned structures.