Quick, Efficient Conversion of Phenones to Conjugated Trienes via Germylene Cycloaddition

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Summary: The germylene Ge[CH(Si(CH$_3$)$_3$)$_2$]$_2$ reacts with phenones to give conjugated trienes. This reaction is quantitative at room temperature in minutes and has some functional group tolerance.

The phenone group, C_6H_5CO, is a common entity in both commercial and natural products. The typically observed chemistry of this fragment includes electrophilic aromatic substitution on the ring and nucleophilic attack at the ketone. However, the array of standard organic methodologies designed to modify the double bonds present in the ring fail to work because of the added stabilization due to aromaticity. A reagent that could break the aromaticity, rapidly generate ene and diene moieties under mild conditions, show functional group tolerance, and do so in good yield could be of great value. We now report that these goals can be accomplished using the germylene Ge[CH(SiMe$_3$)$_2$]$_2$ (**1**).[1,2]

Several intriguing precedents in the literature suggest the mild conversion of a phenone to a conjugated triene might be possible. A conjugated triene species (**A** in Figure 1) is proposed as an intermediate in the reaction between silylenes and phenones.[3−6] However, a 1,3-hydrogen shift of a ring hydrogen to the carbonyl carbon typically reestablishes the aromaticity in the final product (**B** in Figure 1). A notable exception is a recent example where Jutzi et al. isolated a triene product from the reaction of decamethylsilicocene with benzophenone or acetophenone carried out at 50 °C for 3−5 days.[5] Unfortunately, X-ray crystallographic characterization of this unusual fragment was not obtained. We report the synthesis and characterization of a similar class of compounds generated using the stable germylene **1**. In stark contrast to the silylenes, all of the germanium products are stable to the 1,3-hydrogen shift that would reestablish aromaticity.

The chemistry of **1** with phenones leads to the quantitative formation of the conjugated triene species at ambient temperature within 30 min. For example, compound **1** reacts with benzophenone (**2**) in tetrahydrofuran (THF) to produce a bright yellow solution

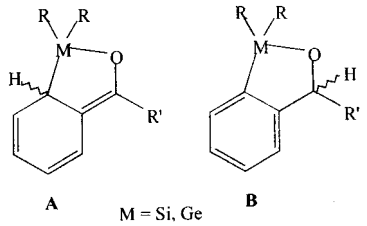

Figure 1. Insertion products before (**A**) and after (**B**) a 1,3-hydrogen shift.

in 3 min. Removal of solvent in vacuo results in a quantitative yield (via NMR) of a yellow solid (**3**).[7] The ^{1}H NMR spectrum contains peaks at 6.790, 6.025, and 5.687 ppm consistent with a conjugated triene and a peak at 3.970 ppm for the ipso CH bonded to the germanium. The IR spectrum exhibits no ν(C═O) or ν(Ge−H). The parent ion observed by FAB-MS (573.3 amu) is also consistent with the proposed structure. Finally, conjugation of the triene to the second phenyl ring results in a yellow color and a visible absorbance with λ_{max} at 412 nm. **1** reacts with isobutyrophenone to give **4**, where no equivalent λ_{max} is observed, due to the shorter conjugation without the phenyl ring. In all, these spectroscopic data suggest the formation of a triene species as illustrated by **A** in Figure 1. The elemental analysis is consistent with this hypothesis.

Propiophenone reacts with **1** in a similar manner to form a white solid (**5**). A suitable single crystal for X-ray crystallographic analysis was grown by slow evaporation from benzene solution, and the assignment of the triene structure was confirmed (Figure 2). An equal mixture of two different enantiomers was present in the *Pca*2$_1$ space group. Alternating double and single bonds for the conjugated triene were observed. The new conjugated double bonds are forced out of planarity, with dihedral angles of 15 and 20°. The angle C6−C7−C2 has become 112.2(4)°, indicative of the sp^3 hybridization

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(7) Benzophenone (141 mg, 0.774 mmol) was added to **1** (300 mg, 0.766 mmol) in 8 mL of THF. A bright yellow solution was immediately formed. The solution was stirred for 15 min, and the volatiles were removed in vacuo. The residue contained the product along with the excess benzophenone. Cold recrystallization in a dry ice/2-propanol bath from acetonitrile afforded 183 mg of analytically pure product (41.6% yield). ^{1}H NMR (C_6D_6): δ 7.75 (d, $^3J_{HH}$ = 8.0 Hz, 2 H, *o*-Ar *H*), 7.18 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, *m*-Ar *H*), 7.06 (t, $^3J_{HH}$ = 7.2 Hz, 1 H, *p*-Ar *H*), 6.79 (dm, $^3J_{HH}$ = 10.0 Hz, 1 H, C*H*), 6.03 (m, 2 H, C*H*), 5.69 (m, 1 H, C*H*), 3.97 (s, 1 H, C*H*−Ge), 0.31 (s, 9 H, TMS), 0.24 (s, 9 H, TMS), 0.23 (s, 9 H, TMS), and 0.16 (s, 11 H, TMS, 2SiC*H*Ge). ^{13}C NMR (C_6D_6): δ 154.49 (*C*−O); 136.81, 128.45, and 128.31 (Ar); 126.40, 126.05, 124.96, 120.08, and 111.63 (*C*═*C*); 38.73 (*C*H−Ge); 13.72 and 11.92 (Si*C*HGe); 3.74, 3.49, 3.40, and 3.05 (TMS). IR: no Ge−H or C═O. GC/MS: showed Ge(CH(TMS$_2$)$_2$ and benzophenone only. UV/vis: λ_{max}412 and 239 nm. Anal. Calcd for $C_{27}H_{48}GeOSi_4$: C, 54.56; H, 8.43. Found: C, 54.53; H, 8.48. FAB/MS: M$^+$ at *m*/*z* 573.3.

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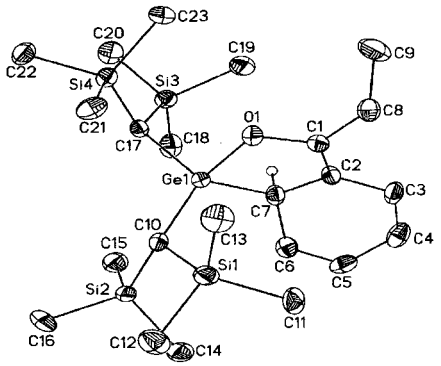
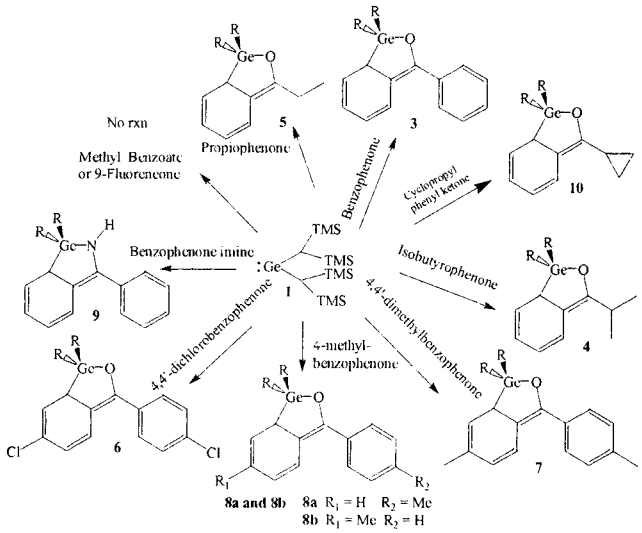


Figure 2. ORTEP diagram of **5**. Selected bond angles (deg) and distances (Å): Ge1−O1, 1.857(3); Ge1−C7, 1.981(5); C1−C2, 1.366(7); C2−C3, 1.448(8); C3−C4, 1.349(7); C4−C5, 1.455(8); C5−C6, 1.338(7); C6−C7, 1.498(7); Ge1−O−C1, 109.9(3); C1−C2−C7, 117.3(4); C7−Ge1−O1, 90.51(18).

Scheme 1. Reactions of 1 with a Variety of Phenones



at C7. The small O−Ge−C7 angle of 90.51(18)° may be due to the steric bulk of the ligands.

A number of other phenone species yield products similar to **2** and propiophenone (Scheme 1). Interestingly, the electronic effects induced by substitution on the ring cause only subtle differences in the formation of the product for many examples. The reaction occurs with both weakly electron withdrawing and releasing groups present on the rings (4,4′-dichlorobenzophenone and 4,4′-dimethylbenzophenone respectively forming compounds **6** and **7**). Also, a mixture of products, **8a** and **8b** in a 1.4:1 ratio, is observed in the reaction of **1** with 4-methylbenzophenone, suggesting the unsubstituted ring is the thermodynamically favored product (*vide infra*). Curiously, 9-fluoreneone and methyl benzoate do not react with the germylene, although the phenone moiety is still present. Finally, since germylenes can insert or undergo other reactions with C−X[1,8−12] or N−H bonds,[1,12,13] it makes the functional group tolerance of **1** with 4,4′-dichlorobenzophenone and benzophenone imine more noteworthy. In each case, rather than undergo insertion, the germylene instead exclusively activates the aromatic ring, forming compounds **6** and **9**.

The phenone activation is reversible. During attempted purification via sublimation of **3** at 90 °C, both germylene and **2** were separately observed in NMR spectra of the sublimate and residue. Separately, injection of any of the germylene−phenone reaction products into a GC/MS instrument results only in the elution of the phenone **1**. Exchange reactions also support the reversibility of the reaction. The placement of **3** in a solution with propiophenone yields **5** and free **2**. Starting with compound **5** and **2** led to the same product ratio, demonstrating the presence of an equilibrium. Addition of benzil to a benzene solution of **3** yields trapped germylene and free **2**.[14]

Molecular modeling calculations have been performed to explore the comparative energetics of the products formed. A noteworthy comparison is the energy of the activated triene with the aromatic product resulting from the 1,3-hydrogen shift. DFT calculations performed at the pBP/DN*[15] and Becke 3:LYP/LACVP**[16] level of theory indicate that isomer **B** (Figure 1) is more stable than isomer **A** by 21−25 kcal/mol for compound **3**, suggesting that **3** is a kinetic product that could undergo the 1,3-shift upon heating. However, only reversion to reactants is observed experimentally in the absence of solvent. This implies the kinetic barrier to reversion must be significantly lower than that for the 1,3-shift.

DFT calculations also suggest the formation of the conjugated triene is enthalpically more stable than the phenone and germylene independently.[15] By comparison of the product energy versus the reactants, it can be determined that the reactions of **1** with **2**, 4,4′-dimethylbenzophenone, 9-fluorenone, and isobutyrophenone lead to products that are 10.2, 8.7, 3.9, and 2.4 kcal/mol, respectively, more thermally stable that the individual reactants. Since the 9-fluorenone reaction is thermodynamically favorable, there must be some other reason that the reaction does not occur, possibly an unfavorable transition state. Calculations for methyl benzoate suggest an increase of 19.2 kcal/mol, likely the reason no reaction is observed. Similar calculations predict that, for 4-methylbenzophenone, **8a** is 0.7 kcal/mol more favorable than **8b**. This suggests a 3.3:1 ratio of **8a** to **8b**, somewhat larger than the experimentally observed ratio of 1.4:1.

Initially, there are a few viable mechanisms for the addition of the germylene to a phenone moiety. In addition to a concerted 1,4-addition mechanism, dipolar, single electron transfer (SET) or diradical mechanisms are possible. If one considers a single resonance form

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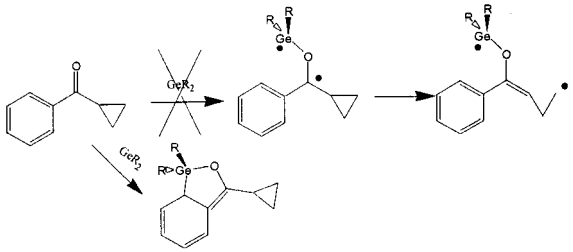
Scheme 2. Reaction of 1 with Cyclopropyl Phenyl Ketone



of the phenone, one of the double bonds is located β to the carbonyl poised for the 1,4-addition typical of dimethylgermylene with vinyl ketones.[17] The dipolar, SET, and diradical mechanisms seem unlikely upon consideration of the reaction of **1** with cyclopropyl phenyl ketone (Scheme 2) to form **10**. The development of either a positive charge or a radical on the carbonyl carbon should lead to ring opening of the cyclopropyl ring.[18,19] Since products derived from the opening of the ring are not observed, the dipolar, SET, and diradical mechanisms appear improbable. Further support for a concerted reaction comes from exploring the reaction of **1** with **2** in THF, diethyl ether, benzene, and hexanes. This leads to the observation that the reaction proceeds at the same rate in each solvent, a characteristic consistent with concerted or radical mechanisms but inconsistent with dipolar or SET mechanisms.

In summary, the reaction of stable germylene **1** with the phenone functional group provides a facile method for converting a phenone into a conjugated triene fragment in high yield and purity. The reaction has been shown to be tolerant of the presence of some functional groups.

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Supporting Information Available: Text giving full experimental and spectroscopic details for all compounds reported. This material is available free of charge via the Internet at http://pubs.acs.org.

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